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THE ACID-BASE EQUILIBRIUM OF THE BLOOD IN CIRCULATORY STASIS.

Experimental and clinical study.

by

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SUMMARY.

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EXPERIMENTAL AND CLINICAL STUDY.

I INTRODUCTION.

Of late years the interest in acidosis has greatly increased. Since the work of NAUNYN, its scope has spread in a remarkable manner, and its study at present holds one of the most important places in pathology. We owe it to physiology, and the pathology of acidosis can only be well understood if some physiological data support it.

But the problems which this study raises are numerous and vast that their mere outline would exceed the limits of this thesis. Therefore, I shall content myself by pointing out rapidly the physiological ideas strictly necessary for a comprehension of the subject.

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The gases of the blood are not only in solution, they are also, and principally, in combination,- the oxygen with the hoemoglobin,- the carbonic acid with the salts of plasma and of the red cells to make bicarbonate. But these combinations vary in magnitude according to the pressure of these gases to which the blood is submitted, and that mathematically. The graph of the combination of these gases with the blood is called the curve of dissociation of the carbonic acid and of the oxygen.

If we put as abscissae the partial pressure of

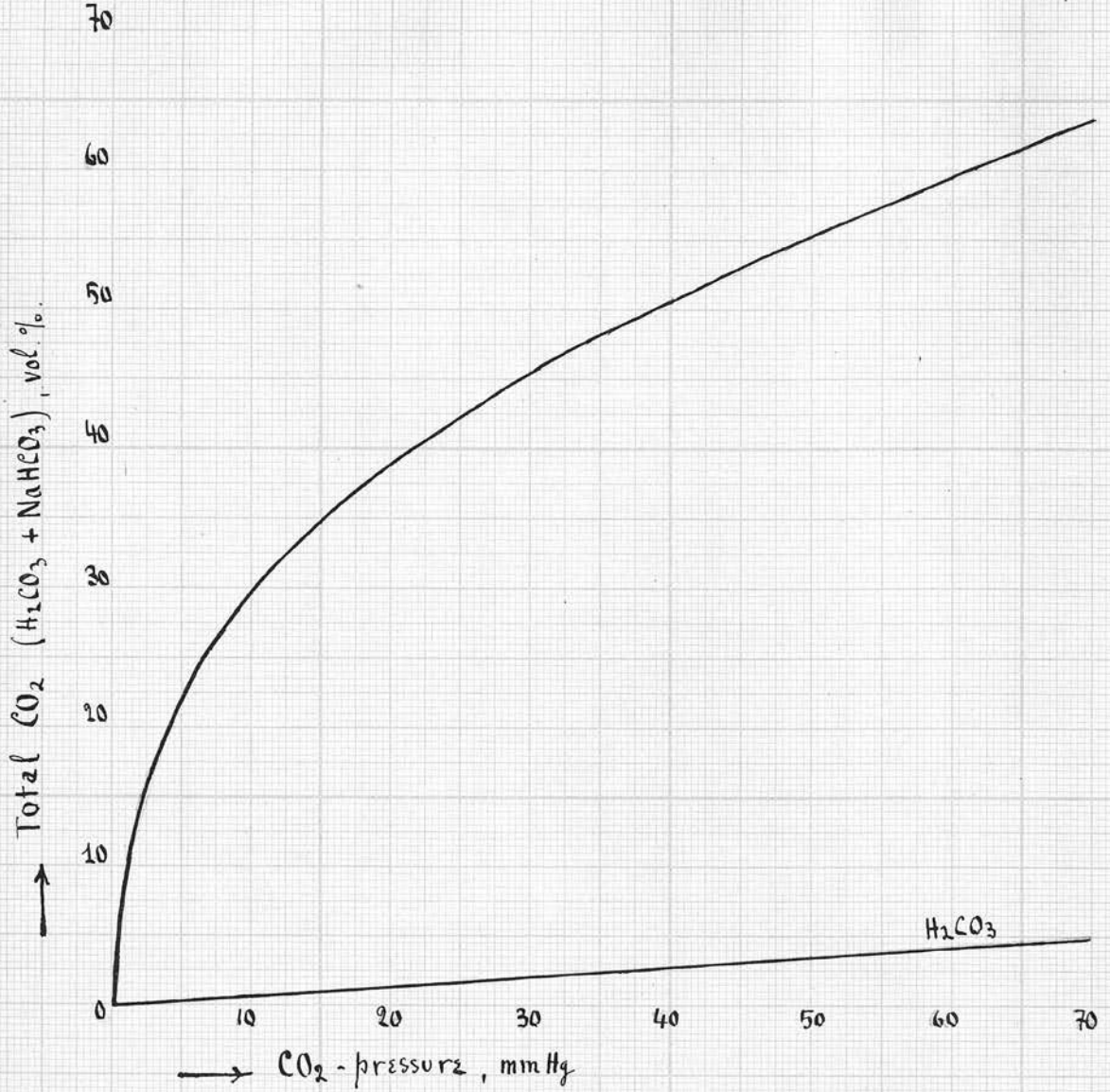

Figure 1

CO_2 dissociation curve
normal blood (HALDANE.)

carbonic acid to which the blood is submitted, and as ordinates the total quantity of carbonic acid, i.e. dissolved and combined (H_2CO_3+$NAHCO_3$) which the blood contains, we obtain the curve which is represented in figure I (CHRISTIANSEN, DOUGLAS and HALDANE (I)). We see that it has the form of a perfect rectangular hyperbola and that, at the pressure of 40 mmHg, the blood contains 5I volumes per cent of total carbonic acid. Measured at the physiological pressures of CO_2 this curve represents the "Alkaline Reserve" of the body. (VAN SLYKE and CULLEN (2)).

In every bicarbonate solution, and, consequently in the blood, there is always some carbonic acid in simple solution. This quantity of dissolved carbonic acid depends (according to the law of solubility of gases (law of HENRY), upon the pressure of that gas to which the blood is submitted, and it is represented in figure I by the lower oblique line marked H_2CO_3. At each point of the curve there is, therefore, a fixed relation between the dissolved carbonic acid (H_2CO_3) and the combined carbonic acid ($NAHCO_3$).

On the other hand, it is well known that the blodd is slightly alkaline; its pH evolves at about 7,35. But this pH is regulated in the last analysis by the relation $\frac{H_2CO_3}{NAHCO_3}$ (L.J.HENDERSON (3)). In other words, for a given pH, the carbonic acid relation to the bicarbonate will always be of the same magnitude. This signifies that, for a given ratio $H_2CO_3/NAHCO_3$ the pH will always be the same, whatever should the height of the curve of dissociation be. This relation of the carbonic acid to the bicarbonate can be roughly

estimated at 3/60 or I/20 in the plasma.

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Let us now come to the modifications, pathological or experimental, of this relation. Each time that the acid radical is increased relatively to the basic radical we find ourselves in the presence of an "acidosis" whatever be the concentration of the bicarbonate. If the basic radical, whatever be its concentration, is relatively increased more than the acid radical we have to deal with an "alkalosis".

The acidosis itself can arise from a primary raising of the numerator. It is called "gaseous acidosis" (4) and it is met with in pathology in the spasm of the glottis, bronchial obstruction, acute bronchopneumonia (5), the administration of morphia (6), the crisis of generalised asthma (5), open bilateral pneumothorax (non published), extensive pulmonary tuberculosis (7), and pulmonary emphysema (8). It is easily reproduced by the experimental respiration of an air charged with carbonic acid (9).

The acidosis can also proceed from a primary lowering of the denominator. Then it is a question of a "non-gaseous acidosis" a type of which is supplied by the diabetic acidosis (I0), (II), (I2), (I3), (I4), (I5), (I6), and violent muscular excercise (I). It is also met with in certain cases of nephritis (I7), (I8), (I9), (20), (2I), (22), in certain cases of enteritis (23), (24), (25), in the course of cyclical vomiting of children, in prolonged fasting (26), (27), (28), (29), (30), (3I), (32), in pregnancy (33), (34), (35),

(36), in intractible vomiting of pregnancy (37), (38), (39), (40),.

If the numerator primarily diminishes, if the acid radical decreases, it is a question of a "gaseous alkalosis". It occurs in the case of the voluntary pulmonary overventilation where much dissolved carbonic acid is expelled (4I), or in overventilation caused by the want of oxygen (42).

Finally, a primary raising of the basic radical (denominator) is called "non-gaseous alkalosis". It is easily produced by the ingestion of alkali.

Such are the four ways by which the acid-base equilibrium can be upset. Nevertheless the organism defends itself in these different contingencies. If it is true that, in the normal state with the healthy subject at rest, apart from the meals, the arterial pH is of a remarkable steadiness, in the pathological state different functional mechanisms intervene which all tend to restore the pH to the normal, by making the denominator follow the same route as that followed by the numerator, and vice-versa. In the gaseous acidosis the basic radical is increased secondarily; in the non-gaseous acidosis the acid radical follows secondarily the primary fall of the denominator; in the gaseous alkalosis the denominator follows the primary fall of the numerator and vice-versa in the non-gaseous alkalosis. In this way the ratio $\frac{H_2CO_3}{NAHCO_3}$ tends to remain constant (I/20) whateyer the level of the bicarbonate and whatever the height of the curve of dissociation may be.

Now let us place ourselves at the point of view

of the living organism taken as a whole. In the physiological state with the healthy subject in complete repose, between meals, the arterial pH is of a remarkable steadiness; it is the same with the quantity of bicarbonate contained in the arterial blood. If we say constant pH and constant bicarbonate we say constant relation between the bicarbonate and the dissolved carbonic acid. From this it follows that the free carbonic acid which is found at the level of the deep pulmonary alveoli and which depends upon the quantity of dissolved carbonic acid is itself constant. Indeed the alveolar carbonic acid, of the resting healthy subject, possesses an average constant pressure of from 39 to 40 mmHg (HALDANE et PRIESTLEY (43)) and the arterial blood contains on an average 5I volumes % of total carbonic acid. These figures, therefore, agree with those we find on the curve of dissociation where 5I volumes % correspond to 40 mmHg.

In the gaseous acidosis this alveolar CO2 is raised primarily and the arterial bicarbonate is increased secondarily; in the gaseous alkalosis it is decreased primarily and the arterial bicarbonate is decreased secondarily. In the non-gaseous acidosis the alveolar carbonic acid follows the denominator and it is decreased. The same happens in the non-gaseous alkalosis and it is increased.

But what are the mechanisms by means of which the organism struggles against all modifications of the pH They are of two orders.

At first the blood itself possesses certain

TABLE I.

representing the chief buffers that maintain the constancy of the blood pH.

PLASMA	Cell wall	CELL
(1) $H_2CO_3 + NaCl \rightarrow NaHCO_3 + HCl$	$\rightarrow HCl \rightarrow$	(3) $HCl + K_2HPO_4 \rightarrow KH_2PO_4 + KCl$
(2) $H_2CO_3 + Na\,protein \rightarrow NaHCO_3 + H\,protein$		(4) $HCl + KHbO \rightarrow HHbO + KCl$
		(5) $HCl + KHb \rightarrow HHb + KCl$
	$\rightarrow H_2CO_3 \rightarrow$	(6) $H_2CO_3 + K_2HPO_4 \rightarrow KH_2PO_4 + KHCO_3$
		(7) $H_2CO_3 + KHbO \rightarrow HHbO + KHCO_3$
		(8) $H_2CO_3 + KHbO \rightarrow HHb + KHCO_3$

Na protein is used to indicate the total alkali salts of the plasma proteins
H protein " " " " the free protein not combined with base.
KHbO and HHbO " " " the alcali salt of oxyhaemoglobin and the haemoglobin not combined with alkali, respectively.
KHb and HHb are used similarly for reduced haemoglobin.

regulating functions. They are summed up in Table I which is borrowed from VAN SLYKE, and which, in the present state of our knowledge, is rather complete.

Let us suppose that some carbonic acid penetrates the blood. It will encounter at first the basic radical of the proteins of the plasma which gives up in this manner a new quantity of bicarbonate; the same phenomenon will be reproduced in the red corpuscles at the expense of the hoemoglobin, the oxyhoemoglobin and the phosphates. Besides, and this is a phenomenon of much greater importance, the carbonic acid extracts the sodium from a salt of a strong acid, as NACL, leaving free the hydrochloric acid which passes into the red corpuscles and which combines with the phosphates and the hoemoglobin. This is what is called the GURBER-HAMBURGER (44, 45) phenomenon from the name of the authors who were the first to bring it to light. This phenomenon has in the course of time been very completely studied by numerous writers (VAN SLYKE and CULLEN (2), FRIDERICIA (46), DOISY and EATON (47), DAUTREBANDE and DAVIES (48).

Therefore we see the whole importance of this transfer of electrolytes which allows the plasma, under the influence of an increased pressure of the carbonic acid and by means of the red blood cells (which cannot supply it directly from the bases) to increase its concentration in bicarbonate.

Table I to be inserted here.

When, inversely, the voluntary overventilation primarilly expels the carbonic acid, thus causing a

diminution of the relation H2CO3/NAHCO3, the inverse phenomenon is present; the arrows on Table I are directed towards the left and the ions CL pass back into the plasma.

By this mechanism the blood itself can struggle against the fall or raising of the pH, actuated by the increase or decrease of pressure of the carbonic acid. It already tends by its own means to restore the relation H2CO3/NAHCO3, to the normal.

But this is not sufficient to restore the pH exactly to the starting point. The blood does nothing but minimise the acidosis or the alkalosis. Functions od another order must intervene to compensate for the original trouble. These functions depend, for the greater part, on the respiratory centre and the urine.

Let us take the example of the non-gaseous acidosis, where there is a primary fall of the bicarbonate. For a short time, notwithstanding the action that we have just studied of the buffers of the blood, there will be relative increase of the pressure of the dissolved carbonic acid, of the numerator of the fraction, and therefore a decrease of the pH; excited by this increase of the H ion concentration, the respiratory centre will clear the blood (by an increased pulmonary ventilation) of the excess of free carbonic acid. The alveolar CO2 will be lowered and in this way, the relation H2CO3/NAHCO3, and consequently the pH, will return to the normal. From 3/60 which the relation was, it will decrease to 2/40 for instance, but it will remain I/20. The acidosis is said to be "compensated".

Now let us suppose that the respiratory centre is

found in presence of a non-gaseous alkalosis, as after the ingestion of bicarbonate or of alkaline phosphates. The arterial blood will be found to be more alkaline than normally, the denominator of the fraction being for the moment increased in comparison with the numerator. To fight against this non-gaseous alkalosis the volume of inhaled air will diminish, the respiratory centre will thus hold back some carbonic acid and the alveolar CO2 will be raised, which will tend to restore the acid-base relation to normal.

But the respiratory centre is not the only one to intervene in order to maintain the pH of the blood normal; the urines themselves play an extremely important part, although apparently less rapid. The urine is generally acid although coming from an alkaline blood; the kidneys therefore play the part of separating the acids from the blood to make them pass into the urine. But the acidity of the urine (measured by the pH, or better by the quantity of titrable acids) increases in the acidosis, thus leaving to the blood more bases to fight against the elevation of the H ion concentration. In alkalosis the acidity diminishes or makes place for the alkalinity, which tends to lower the basic radical primarily too high. (DAVIES, HALDANE and KENNAWAY (4I)).

Finally the urinary ammonia intervenes. Its value can serve as an index of the blood's reaction. The ammonia in solution has alkaline properties which permit it to neutralise the acids. If we give to an animal a certain quantity of mineral acids, or if we make it breathe an air charged with carbonic acid we see the quantity of urinary NH3 increase considerably. If we

give to an animal a certain quantity of bicarbonate, the urinary ammonia disappears. This is also the case after a forced overventilation of some duration which brings about a sufficient expulsion of free carbonic acid to cause an acute gaseous alkalosis (DAVIES, HALDANE and KENNAWAY (4I), HALDANE, KELLAS and KENNAWAY (42), HASSELBACH and LINDHARD (50). The quantity of urinary ammonia (increased in acidosis and decreased in alkalosis) can therefore give an idea of the blood reaction, as well as the ratio NNH3/NUREA still called "ammonia index". This relation is increased in the acidosis; from 5 which it is normally it can reach 50; it is decreased in the alkalosis.

By these different mechanisms (buffers of the blood, respiratory centre, kidneys) the carbonic acid-bicarbonate relation remains constant, whatever be the actual concentration in bicarbonate. In other words, this relation can be 2/40, 3/60, or 4/80, the pH is unchangeable if it remains at I/20.

In summing up, therefore, acidosis, whether gaseous or non-gaseous, is characterised by a relative increase of the numerator of the fraction $\frac{H2CO3}{NAHCO3}$ and alkalosis by a relative increase of the denominator, whether this alkalosis be gaseous or non-gaseous. This acidosis and this alkalosis are weakened at first by the play of the buffers in the blood itself, then in the course of time and principally by the intervention of the respiratory centre and the kidneys. These different mechanisms tend to do away with the primary trouble of the acid-base equilibrium.

Such are briefly the principal points of the physiology of the acid-base equilibrium of the blood.

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However, since I922 another kind of acidosis must be added to the nomenclature, i.e. the "circulatory acidosis".

The greater part of the physiological eventualities considered up to the present rested upon a modification of the acid-base equilibrium in the organism considered as a whole. The diabetic acidosis is an acidosis common to all the tissues and to the blood in different parts of the body. So it is of the gaseous acidosis of the experimental respiration of an air charged with carbonic acid. The non-gaseous alkalosis of the ingestion of bicarbonate is an alkalosis uniformly distributed in the whole body.

Nevertheless, localised troubles of the acid-base equilibrium exist. Furthermore, an acidosis can exist at the same time as an alkalosis at different places. Of this the cardio-respiratory pathology offers numerous examples for a long time unknown. In order to be better able to place the characteristics of the physiological conditions in which this particular situation exists it will be useful to turn chronologically to the different researches made upon the ionic equilibrium in affections of the circulation. That will serve at the same time as a history of the question.

I) All the Writers have always been in agreement in saying that in the decompensated cardiac affections the alveolar air, on account of dyspnoea, was poor in

carbonic acid (BEDDARD and PEMBREY (5I), FITZGERALD (52), PORGES LEIMDORFER and MARKOVICI (53), LEWIS, BARCROFT and their collaborateurs(I9), PEABODY (I8), PETERS and BARR (54), PETERS (55), CAMPBELL and POULTON (56), MEAKINS DAUTREBANDE and FETTER (57), DAUTREBANDE (58)) and that it again became normal after recompensation.

2) NEWBURY, PALMER and HENDERSON (59) have found on the other hand with the decompensated cardiac patients the urinary pH lowered; it would again become normal after recompensation.

3) LEWIS, BARCROFT and their collaborators (I9), studying the oxyhoemoglobin dissociation curve of venous blood (which varies in height according to the blood's reaction) conclude that there is an acidosis which they attribute to the formation of lactic acid. Nevertheless, they admit that the quantity of lactic acid found in the blood and urine is not sufficient to explain the dyspnoea.

4) Finally, PETERS and BARR (54) find the curve of dissociation of the carbonic acid in the venous blood lower than normally during decompensation. It rises again after recompensation. It can moreover be seen from their figures that the venous pH was clearly lowered during the decompensation.

From the preceding four points, the writers have generally concluded that there is an acidosis and this is exact so far as we keep to the venous blood. But

5) HARROP (60) affirms the poorness of the arterial blood in total carbonic acid during the decompensation. After recompensation it returns to a normal level. These facts are confirmed by the writers who have

studied the arterial blood of cardiac patients. (CAMPBELL and POULTON (56), PETERS and BARK (54). 6) This fall has every signification when we compare it with the results of FRASER, ROSS and DREYER (6I) who find in the arterial blood of cardiac subjects a pH much higher than in that of healthy subjects: an alkalosis. This alkalosis disappears after recompensation.

This evidently seems in contradition with the preceding facts (+). Nevertheless, this paradox of the venous acidosis and the arterial alkalosis is only apparent; these two phenomena are perfectly reconciliable and actually explained.

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In studying the modifications of the acid-base equilibrium of the blood of patients suffering from mitral stenosis of which the blood flow was greatly diminished, MEAKINS, DAUTREBANDE and FETTER were struck, as CAMPBELL and POULTON, PETERS and BARR, with the fact that, if one placed the value of the total carbonic

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(+) On the other hand the results of HARROP, FRASER, ROSS and DREYER were not to be trusted for the fundamental reason that not one of these writers had taken into account the oxyhemoglobin saturation of the arterial blood before making a primary alteration of the acid-base equilibrium responsible for the fall of the CO_2 and increase of the arterial pH. With the greater number of HARROP's patients the signs of pulmonary decompensation could be clinically disclosed and the arterial blood was often considerably desatured of oxygen. We know that the anoxemia alone causes overventilation and secondarily alkalosis.

acid of the arterial blood upon the curve of dissociation obtained by means of venous blood, the pressure thus found did not at all correspond with the alveolar pressure of the carbonic acid (decreased on the other hand in all these subjects). These patients on the other hand expelled their alveolar air correctly.

But if instead of utilising the venous blood of the arm to construct the dissociation curve arterial blood was used, the alkaline reserve was found much higher than in the venous blood, and , in these conditions, in placing opposite the alveolar pressure of the CO2 the figure of total carbonic acid found in the arterial blood, it fell exactly upon the dissociation curve of this blood.

In these conditions however the arterial blood was in a state of non-gaseous alkalosis through a deficiency of free carbonic acid due to the overventilation. This alkalosis became prominent during the periods of auricular fibrillation always accompanied by a more considerable slowing of the blood flow.

The venous blood of the arm possessed a considerable pressure of free carbonic acid; by reason of this fact, and of the fall of the curve of dissociation, it was more acid than normally. Consequently the difference existing between the arterial pH and the venous pH was exaggerated.

Finally, in the generality of cases the venous blood was much richer in hoemoglobin than the arterial blood.

The prevailing phenomenon, and which, up this time, had misled the experimentalists was therefore the exis-

tence of a venous alkaline reserve lower than the arterial one.

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Till now we have seen that an eventuality could lower the curve of dissociation of blood in a state of acidosis, namely the primary alkali deficit of which the acidosis is the type. In the stasis conditions the curve of dissociation can decrease by another mechanism studied by DAUTREBANDE, DAVIES and MEAKINS (62).

We know that, if we submit the total blood to the action of carbonic acid, the plasma is enriched in bicarbonate, particularly through the secondary buffering of the red cells, that is to say, by means of the passage of the CL ions of the plasma towards the corpuscles, the remaining NA combining with the carbonic acid to form supplementary bicarbonate. On the other hand, in the physiological conditions, the plasma always contains more bicarbonate than the red cells. Therefore it follows that, if from the centrifuged blood under paraffin we draw a certain quantity of plasma, and replace the remaining blood (that is to say the intact quantity of corpuscles + the plasma diminished in volume by the quantity drawn off) in presence of a given pressure of carbonic acid, the alkaline reserve of the blood so treated will evidently be diminished. The more plasma drawn, and the more bicarbonate in the plasma, the more it will be decreased. This latter value depends principally upon the pressure of carbonic acid to which the blood is submitted and subsequently upon the passage of the chlorides into the corpuscles.

These conditions are reproduced in vivo by the local experimental stasis (DAUTREBANDE, DAVIES and MEAKINS (62). If by means of a tourniquet the arm is submitted to a prolonged severe stasis, the venous blood which returns from it has its dissociation curve and its pH greatly decreased and it is considerably enriched in hoemoglobin.

But, as this blood was much desaturated with oxygen and as want of oxygen, according to FLETCHER and HOPKINS (63) and BARCROFT (64) and his collaborators, can cause the formation of lactic acid, one might wonder if the decrease of the alkaline reserve was not simply due to this lactic acid. However this was not the case: the blood returning from the parts in stasis did not contain any more lactic acid than the normal venous blood.

The cause of the acidosis is elsewhere and this is how we can briefly sum up the different stages of the phenomenon.

Under the influence of the slowing of the circulation the free carbonic acid is accumulated in the blood, hence transfer of CL of the plasma towards the corpuscles and enriching of the plasma in bicarbonate. At the same time the blood becomes concentrated in hoemoglobin by the fluid of the plasma passing towards the tissues; the blood can in this manner lose more than 20 % of its water. But this passage of water from the plasma towards the tissues is accompanied by a passage in the same direction of chlorides and bicarbonate, which causes the decrease of the alkaline reserve. Consequently,

other things equal, the decrease of the alkaline reserve is all the more pronounced as the quantity of bicarbonate in the plasma is considerable, and as primarily the pressure of the carbonic acid in the blood in a state of stasis will be increased since the greater the pressure of the free carbonic acid the more the plasma is enriched in bicarbonate (+).

From these experiments it follows that I) the concentration of the blood in hoemoglobin 2) contemporary with an increase of local pressure of free carbonic acid 3) decreases the alkaline reserve 4) by passage from the blood towards the tissues, of water and salts among which is bicarbonate.

It is to this mechanism that we must attribute the acidosis of the decompensated cardiac patients, and this explains why different writers have come to the conclusion that the blood of those subjects was more acid than normally. That is absolutely correct for the blood returning from the parts of the body in a state of stasis.

But it is none the less true that the arterial blood of these patients is in a state of alkalosis. During the decompensation their blood flow is diminished; instead of 7 litres per minute (average generally admitted in healthy resting subjects ~~, DOUGLAS and HALDANE (65), HENDERSON (66), MEAKINS and DAVIES (67)) the heart does not deliver more than 5, 4, 3, or even 2 litres. The organism is then in a state of stasis

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(+) These experiments were the first to show the existence in vivo of the GURBER HAMBURGER effect.

and the respiratory centre will suffer from an acidosis through accumulation of carbonic acid similar to that which has just been described. But the respiratory centre responds, as we know, to the least increase of the H ion concentration by means of overventilation. It follows that the lungs, in expelling an exaggerated quantity of free carbonic acid cause a decrease of the alveolar carbonic acid, whence a decrease of the numerator of the fraction H2CO3/NAHCO3 in the arterial blood (gaseous alkalosis). On the other hand, on account of the stasis, even if the arterial blood is well saturated with oxygen, the respiratory centre may suffer from oxygen want which acts, as to overventilation, in the same way as the accumulation of carbonic acid. This stasis and this need of tissue oxygen obviously explain the cyanosis of the extremities met with in cardiac patients free from any sign of pulmonary decompensation.

Such are the characteristics of this new kind of acidosis which we can rightly call circulatory acidosis since, as we are going to see, it is found in all pathological or experimental conditions characterised by a circulatory slowing.

But it was evidently necessary, in order to confirm this theory, that the different phenomena described should be found in other states of stasis than those primarily studied by MEAKINS, FETTER and myself, whatever be the origin of that stasis. It was also necessary to find this decrease of the alkaline reserve and this venous acidosis in some states of experimental stasis other than that caused by the tourniquet (perhaps too severe).

On the other hand, if the hypothesis were true, the curve of dissociation of the arterial blood would have to decrease in its turn during the production of oedema sufficiently large or sufficiently prolonged to diminish the total quantity of circulating bicarbonate. Finally, contrary to the first experiment, it was necessary to observe the circulation after the disappearance of the stasis and to assure one's self at that moment of the return of the acid-base equilibrium to the normal.

This thesis will be the object of the study of these different points.

II METHODS.

No examination has been made without a lengthy preliminary training of the different subjects so that their intelligent and continued collaboration was assured.

All the subjects were in a complete state of rest, in a sitting position for at least half an hour before the examination, in a room at a uniform temperature of from 18° to 20° centigrade, at least three hours after a light meal.

I) ALVEOLAR AIR. The alveolar air was taken by the HALDANE-PRIESTLEY (43) method. Each figure given is the average of at least four samples of which two were taken at the end of a normal inspiration, and two at the end of a normal expiration.

2) EXPIRED AIR. The expired air was taken in a DOUGLAS bag by means of the mask described by DAVIES and myself (68). This mask has the advantage of not causing any resistance to the respiration (DAUTREBANDE

and DAVIES (68), DAUTREBANDE (69)) which is of the greatest importance for the observation of the cardiac patients whose respiration is already laborious in itself. The expired air, as the alveolar air, were analysed by means of HALDANE's small apparatus.

3) BLOOD FLOW. The blood flow was determined by the method of MEAKINS and DAVIES (67). It consists essentially of three phases: A) determination of the arterial tension of the carbonic acid by means of the alveolar pressure of this gas; B) determination of the tension of the carbonic acid of the mixed venous blood coming from the right side of the heart; C) determination of the quantity of carbonic acid expired in unit time. Knowing the difference of pressure between the arterial carbonic acid and the venous carbonic acid, it is easy to know, by means of the curve of dissociation of the carbonic acid in the blood (fig. I), the quantity of this gas which one hundred volumes of blood lose during the passage through the lungs. Knowing, on the other hand, the quantity of carbonic acid expired per minute, one has only to divide the latter value by the first in order to obtain the blood flow in litres per minute.

To determine the quantity of corresponding carbonic acid in the arterial and mixed venous blood at the pressure of the carbonic acid of the gases taken by the HALDANE-PRIESTLEY and MEAKINS-DAVIES method respectively, we can use the curve of dissociation of the blood of HALDANE (fig. I) provided that the curve of the subject examined, although higher or lower than this latter, be parallel to it. All the curves of subjects examined were, at physiological pressures (30-60 mmHg), parallel

to the curve of the blood of HALDANE, except that of the subject 8 which was less acute. The blood flow of this patient was calculated by means of his own curve. The blood flow of the other patients was calculated by means of the curve of the blood of HALDANE, made and enlarged by means of PARSONS (7I) formula.

It may be useful, for the comprehension of the subject, to give an example of the different phases of an examination.

SUBJECT I3 24-5-23. Table. XIV.

Alveolar air. at the end of an inspiration 5,74 CO2 %
5,72 " %

" " " " " expiration 5,98 "
6,00 "

Average 5,86 %

Barometer = 754 = 4I,40 mmHg

Volumes % of corresponding carbonic acid according to the curve of dissociation at the pressure of 4I,40 mmHg = 5I,7.

Venous tension of the carbonic acid (mixed venous blood)

7,I9 CO2 %
7,I8 " %
7,23 " %
7,27 " %
7,I7 " %

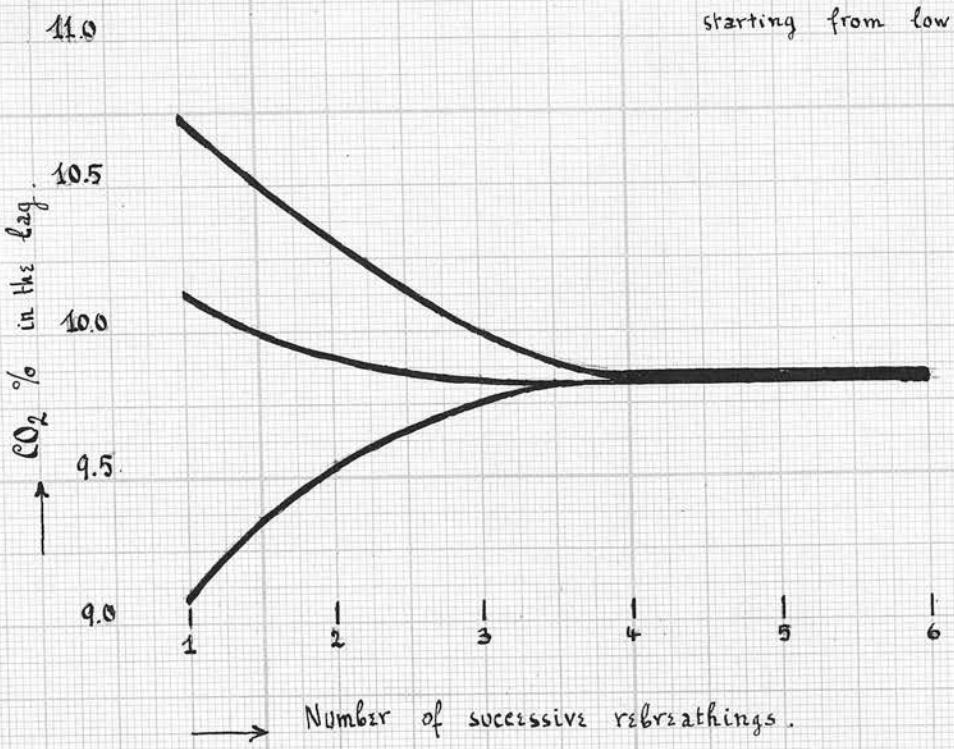
Average 7,20 CO2 % = 50,90 mmHg.

Volumes % of corresponding carbonic acid according to the curve of dissociation at the pressure of 50,90 mmHg = 55,9. Difference: 55,9 - 5I,7 = 4,2 volumes p.c. One hundred volumes of blood lose 4,2 volumes of carbonic acid during the passage through the lungs. One litre then loses 42 volumes.

Expired air. 325 litres per hour. The expired air contains 3,48 % of carbonic acid. The factor of reduction of the air at 0° and at 760 mmHg is, on that day, 0,9245. The quantity of carbonic acid expired per minute is

Figure II

CO_2-tensions of the mixed venous blood, starting from low and high pressures of CO_2.



therefore equal to 325 : 60 = 5,416 litres x 3,45 (3,48 - 0,03 in the atmospheric air) = 173 cm3.

To obtain the blood flow, one has only to divide 173 : 42 = 4,12 litres per minute. The pulse was 68, hence 4,12 : 68 = 60 cm3 of blood per systole.

To obtain the pressure of carbonic acid of the mixed venous blood, the MEAKINS-DAVIES method is, excepting a few variations, the same as the primary methods of DOUGLAS and HALDANE (65), and of HENDERSON and PRINCE (70). It determines this tension by having the patient make successive rebreathings (the duration of each series of rebreathings not exceeding 15 seconds) into a rubber bag containing atmospheric air and an initial percentage of variable CO2 until, after a certain number of rebreathings in a closed space, the percentage of carbonic acid in the air of the bag becomes constant.

In figure II we see the stage at which we arrive after a certain number of rebreathings by proceeding from different levels of carbonic acid. These three curves were obtained in one hour with subject.8.

Figure II

By the examples given, we see the regularity at which we can arrive and the remarkable constancy of the pressure of carbonic acid of the mixed venous blood during a fixed examination.

During the determination of the blood flow, the patient was in a sitting position exactly half an hour before the beginning of the examination. BARCROFT and MARSHALL (72) have indeed noted that the longer the rest

the more decreased was the blood flow. With different patients whose study is not reported, I have never been able to find this decrease of the blood flow by the prolonged rest. One must ask one's self if BARCROFT and MARSHALL have sufficiently avoided a cause of error which I have recently pointed out (58), namely the influence of the meals. A meal sometimes increases by 70 % the blood flow which returns to the normal only 3 hours later. If the determination is made one hour after a meal it is obvious that we shall see under these conditions the blood flow progressively decrease. On the other hand, with the cardiac patients who have already only two litres of delivery per minute, after a rest of half an hour, it is difficult to admit a considerable fall of this value following a more prolonged rest.

4) ANALYSES of the BLOOD. The arterial and venous blood of the arm was analysed in all the subjects. The arterial blood was collected by puncture of the radial or brachial artery under thick liquid paraffin to which were added a little neutral powdered oxalate of potassium and fluoride of sodium to avoid glycolysis and the formation of lactic acid in the blood (C.L.EVANS (73)). The venous blood was collected under the same conditions from a superficial vein of the elbow without the least stasis. Both the arterial and venous blood were analysed from four points of view: A) CO2 - content B) oxyhoemoglobin saturation; C) capacity in oxygen; D) alkaline reserve or capacity of combination of the blood with carbonic acid at different pressures of this gas, in vitro. All the analyses of the gases of the

blood were made by means of HALDANE's latest apparatus (74). The oxyhoemoglobin saturation was calculated by means of the formula: Saturation in oxygen % =

$$\frac{\text{Capacity in oxygen - absorbed oxygen}}{\text{capacity in oxygen}} \times 100$$

The alkaline reserve was determined in the total blood according to the technics of CHRISTIANSSEN, DOUGLAS and HALDANE (I). (+) The hoemoglobin value was calculated by means of the oxygen capacity of the blood, 100 % of Hb corresponding to 18,5 volumes % of oxygen.

5) pH.

The pH was not directly determined but calculated by means of the HASSELBACH (75) formula: pH = pKI + log. $\frac{NAHCO3}{H2CO3}$, 6,1 being taken as value of pKI. H2CO3, that is to say the carbonic acid in solution depends upon the pressure of the free carbonic acid to which the blood is submitted. It is calculated by means of the BOHR formula: $H2CO3 = \frac{0,5II}{760} \times P\ CO2$ (0,5II being the coefficient of solubility of the carbonic acid in the total blood at 38° centigrade; P CO2 being the pressure of carbonic acid to which the blood is submitted and 760 the barometric pressure). NAHCO3 is the difference

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(+) The different curves of each patient were traced by joining the different points obtained through placing the blood in vitro at successive pressures of CO2. To render it easier and not to encumber the tables which are already sufficiently full, only one value of these curves is reported, at 40 mmHg. The whole of each curve will be found in the different figures which accompany the tables.

between the total CO2 and the carbonic acid in simple solution.

We know the arterial pH if we know I) the alveolar pressure of the carbonic acid and consequently the quantity of dissolved carbonic acid, 2) the total carbonic acid which is obtained by direct analysis of the arterial blood.

When one cannot obtain the alveolar air, it is possible to calculate it without noticeable error (at least in the case of gaseous alkalosis as with the cardiac patients) by placing on the curve of dissociation of the arterial blood the figure of total carbonic acid found by direct analysis of this arterial blood.

To obtain the pH of the venous blood a correction is necessary. CHRISTIANNSSEN, DOUGLAS and HALDANE (I) have shown that the reduced blood was, at identical pressures of carbonic acid, more alkaline that the well oxygenated blood, and the more so when the oxyhoemoglobin desaturation was more pronounced. In other words, the dissociation curve of the reduced blood is higher than of the blood rich in oxygen; or again, the reduced blood absorbs more carbonic acid than the arterial blood, at the same pressure of this gas, without pH changing. PETERS, BARR and RULE (76) have calculated that for each volume of oxygen used the blood was capable of absorbing 0,34 vol of carbonic acid without pH changing. DOISY, EATON and CHAMBERS (77) arrive at the figure 0,27. But this value varies with the quantity of hoemoglobin. To calculate the venous pH of the patients studied, the average figure 0,30 has been used.

Here is how we can obtain the true pH of the venous

blood by taking into account the described peculiarity. From the carbonic acid found directly in the venous blood (A) we substract the product 0,30 by the quantity in volumes of oxygen absorbed by the tissues. We obtain a figure (B) of carbonic acid which we carry to the curve of dissociation. Thus we know the real pressure of CO2 to which the blood was submitted. Opposite this pressure we place in ordinates the figure (A) of carbonic acid which corresponds to the real curves dissociation, in the body, of the venous blood studied.

At the different figures the sign • corresponds to the figure of carbonic acid found in the venous blood and placed, without correction, on the curve of dissociation; the sign ■ to the real curve of the blood in the body, opposite to the true pressure of carbonic acid to which this blood was submitted when it was drawn.

III SUMMARY OF THE CLINICAL CASES.

For greater facility, each patient will be indicated by a number.

PATIENT I: A.W., 65 years, admitted at hospital 6.II.24.

Diagnosis: Cardiac decompensation, myocarditis.

No hereditary antecedent. As personal antecedent, declared only a serious quinsy when 9 years of age.

His present illness began two months ago by dyspnea, cough with spumeous expectoration, and lumber pains. His feet had begun to swell six weeks ago; the skin at the level of the tibias was dotted with reddish spots the size of a pin head; the skin at this part was insensitive.

Now the subjective symptoms are the same. Objectively the face and chest of the patient present an icteric tint. The lips, hands, and palate are considerably cyanosed. There is an oedema of the lower limbs reaching to above the iliac crests. There are confluent purpuric spots on the right leg and over the left tibia.

The heart is enlarged in all its dimensions. The pulse is weak, small and frequent (I00 per minute). At the auscultation no murmur is heard. The arterial pressure is of I3 x I5. The teleradiography shows that the heart measures 2I centimetres in its transverse diameter (heart in triangle).

There is dullness of the bases of both lungs with "ronchi" on all the pulmonary surface and moist crepitations at the level of the two bases, but especially on the right. The radiography discloses also an effusion at this level.

The quantity of urine does not exceed 600 ccm per day. It contains some albumen without casts.

The liver is voluminous and painful. It extends to 4 centimetre beyond the false ribs.

Treated with digitalis from 8-II-24, this patient takes 3,5 milligrammes of this medicine in five days. The albumen disappears from the 9-II; the dyspnea diminishes uniformly without, however, disappearing completely. On the I0-II-24, he passes 5 litres of urine; on the II, 6.600 cm3; on the I2,4600; on the I3 3850, then 2000 cm3 regularly. The pulse is at 70 per minute, regular with some extrasystoles. The oedema has diminished, as also the purpura. There are no more rattlings at the bases. A teleradiography on the I4-II-24 shows the disappearance of the pulmonary stasis; the heart measures on the plate only I7 cm. in its transverse diameter.

The patient then takes thirty drops of strophantus tincture per day from the I8th to the 23-II-24. At this time there is an acute attack of auricular fibrillation. The pulse is irregularly irregular in strength and rhythm; the pulse of the wrist is deficient by 40 on the rhythm of the apex of the heart.

From the 24-II-24 to the 3-I2-24, he takes three grammes of sulphate of quinidine and I milligramme of digitalis. The pulse then becomes again regular, 60 at the wrist as at the apex. ~~of the then becomes again regular, 60 at the wrist as at the aspex of the heart.~~ The

oedemas are completly resorberd on the I0-I2-24. There is not pulmonary sign whatever. The liver no longer goes beyond the costal border. Teleradio~~tele~~graphy shows the heart measures only I6 centimetres in its transverse diameter. The patient being cured leaves on the I5-I2-24.

PATIENT 2: C.D., 65 years, admitted to hospital on the I3-I2-24.

Diagnosis: Auricular fibrillation, cardiac decompensation, Emphysema.

No hereditary antecedent. As personal antecedent only declares frequent attacks of rheumatism since the age of 35. The present illness began in April I924. The beginning was sudden. Breathing suddenly became very difficult even during rest; then oedema of the lower extremities appeared. All these symptoms were improved by a digitalisé treatment. In october I924 there was a relapse. For I5 days reddish spots were observed over the tibias on the oedematous skin.

Now, the state is that of a decompensated cardiac; the oppression is considerable, even when resting; there is orthopnea. The patient complains of continuous and spontaneous pains at the level of the liver.

Objectively, the cyanosis of the hands and face is intense. The sclerotics have an icteric tint. The oedema goes as far as the navel. Generalised purpura exist in both legs.

The heart is globulous, increased in size in all its diameters. It measures I9 cm in the horizontal diameter, by teleradiography. The arterial tension is I2 x I5. The pulse is at I00, irregularly irregular in rhythm and strength. The deficiency at the wrist is 40 per minute. There is no perceptible murmur. The liver reaches a height of 22 cm at the level of the mammillary line.

The urine is scanty (600 ccm every 24 hours), and it contains no albumen.

The lungs present nothing special except a stifled breathing on all the thorax surface with abolition of the vesicular sound at the two bases. Radiography shows horizontality of the ribs and large masses of bronchial sclerosis.

From the I7-I2 to the 20th, this patient takes 2 milligrammes of digitalis. The oedema slightly diminishes, but the quantity of urine passed does not exceed I000 cm3 per 24 hours. From the 2Ith to the 25th he takes 30 drops of strophantus tincture per day; from the 26-I2-24 to the 2-I-25, he takes one milligramme of digitalis and 5 grammes of theobromine. The oedemas are completely resorbed after the patient has passed 2000 ccm of urine in several days.

Since then the condition has continually improved; the liver returned to its normal proportions; the pulse is normal in strength and rytlhm; the oedemas do not reappear. The lungs are free but always present signs of emphysema. The teleradiography of the I3-I-25 shows a heart still increased in size but not measuring more than I7 centimetres in its transverse diametre.

PATIENT 3: M.D., 23 years; admitted to hospital 2-2-23.

Diagnosis: Pulmonary tuberculosis; artificial pneumothorax; dextrocarditis.

Neither hereditary nor personal antecedent. He has lost much weight for six months; coughs and expectorates much. The expectoration contains KOCH's bacilli. The reaction of BESERDKA is positive.

The right lung, under the X rays, presents only some disseminated lines with slightly marked bronchial sclerosis and hilus opacity. The left lung is dull all over. On auscultation one perceives moist rales with big crepitations on the whole of this lung and a hollow breathing sound at the apex confirmed by the presence, under radiography, of a cavern the size of a mandarine.

A pneumothorax has been established on the 26-2-25. The collapse was complete from the first insufflation except at the apex where there still exists a strip holding the superior lobe. From the first week of the collapsotherapy there is a marked displacement of the mediastinum which, as radiography enables us to notice, overlaps the vertabral column by 4 centimetres to the right. The heart is greatly thrown towards the right, its apex beats in the sixth intercostal space at the level of the left parasternal line; the left edge is situated at the level of the medial sternal line. There is no cardiac murmur.

This cardiac displacement continued during the whole duration of the pneumothorax. The pulse remained fast notwithstanding the improvement in the general condition and the dyspnea intense at the least effort.

There is nothing to note concerning the other organs except an enlarged liver. It was I7 cm. in the mammerly line. There were neither apparent oedemas nor albumen. This patient never had fever during the two years that the pneumothorax lasted.

PATIENT 4: C.D., 78 years; admitted to hospital on the 20-I-25.

Diagnosis: Chronic myocarditis, Complete arhythmia.

Neither hereditary nor important personal antecedent. For three months the patient feels so short of breath that she is inable to walk. She feels cardiac palpitations, even when resting. The cough is very frequent especially during the night.

At the examination, oedema of the lower limbs up to the level of the knees was found. The cyanosis of the extremities, lips, cheeks and palate is very marked. The pulse is at I20 in complete arhythmia. No murmur is heard. The sounds of the heart are considerably muffled. The heart is greatly increased in size; the apex reaches the anterior axillary line and, on the right, to two fingers beyond the right parasternal line. The arterial tension is II,5 x I5.

The lungs present some stasis râles at the bases. The respiration reaches 38 to the minute.

The lower edge of the liver reaches the umbilicus. The abdomen is very distended without ascites.

The patient passes 2400 cm3 of urine. There is no albumen.

PATIENT 5: G.C., 62 years; admitted to hospital 24-II-24.

Diagnosis: Cardiac decompensation after apoplectic stroke.

Neither hereditary nor interesting personal antecedents. Had an apoplectiq stroke six weeks before with paraplegia of the lower limbs. Since then the patient complains of an intense dyspnea, even in bed.

At the objective examination the heart reaches to the left nipple, and to the right extends by two fingers beyond the right parasternal line. The sounds of the heart are low and muffled. There is no perceptible murmur. The pulse is weak and flowing.

The liver extends beyond the ribs by three fingers at the level of the mamillary line. The urine is scarce (700 cm3 every 24 hours). It contains albumen without cylinders.

The lungs present large stasis râles at the two bases.

The faculty of moving and the sensibility of the two lower limbs are nearly abolished. The knee jerks are exaggerated. The cremasteric and abdominal reflexes are abolished. There is paralysis of the sphincters.

The patient died 5-I2-24

PATIENT 6: G.J., 44 years: admitted to hospital I-I2-22

Diagnosis: Arterio-sclerosis; chronic alcoholism, cardiac insufficiency.

Hereditary antecedents: His father and mother died of cardiac affection. A sister living, also suffers from cardiac affection.

Personal antecedents: The patient mention an attack of acute articular rheumatism when I5 years of age. From 2I to 25 these attacks returned rather frequently

During the war he had bronchitis which became chronic. In I9I7 he had another attack of rheumatism. Finally, since I9I8 attacks of nocturnal oppression presented themselves. The patient is a chronic alcoholic ex-colonial. He drinks from one two litres of wine per day.

On the 2I-I2-22, one finds at the examination the heart in triangle; the left edge reaches to the nipple; the right edge is two centimetres beyond the right parasternal line. The teleradiography confirmed these measurements. The heart measures I7 centimetres in its transverse diameter. Arterial tension I0 x I2.

No ronchi are found in the lungs. The liver is large and hard, and slightly mammelated on the surface. It measures I9 centimetres at the level of the mammillary line.

There is no albumen in the urine.

There are no visible oedemas. The cyanosis is noticeable, even when resting, especially at the level of the lips, finger nails and palate.

PATIENT 7: C. de H., 54 years; admitted to hospital 4-II-24.

Diagnosis: Pulmonary emphysema; bronchial sclerosis; cardiac decompensation.

No striking hereditary antecedent.

As personal antecedent the patient had typhoid, an abscess of the liver (operated), and a purulent pleurisy (not operated), all these illnesses at the age of 4I years.

The present illness dates from I922. It began with bronchitis. From this bronchitis remained a certain dyspneea when effort is made which has not improved since. From last week, it exists even when in a state of rest. For three days the patient has noticed that his feet swell. Muscular weakness is extreme.

Now the patient appears cyanotic, with a purple blue cyanosis. There is oedema of the lower extremities up to the upper third of the femur.

The thorax is rounded and barrel. There is dullness at the left base. The vocal vibrations are abolished on the whole thoracic surface. The vesicular sound has disappeared at the bases. The respiration is low and remote at the apices. There are sibilant ronchi on the entire respiratory surface with moist ronchi (not modified by the cough) at the left base. Under radiography, the horizontality of the ribs is noted (thorax bell-shaped) with a generalised bronchial sclerosis.

The heart is large and globulous. It reaches to the left breast and extends beyond the right parasternal line by I cm. Under teleradiography, it measures I8 centimetres in its transverse diameter. The sounds of the heart are muffled; there is no murmur. The arterial tension is II,5 x I5.

The patient passes 2500 cm3 of urine every 24 hours. The urine contains albumen without cylinders nor figurate elements.

This patient's blood, examined during the present decompensation, could not be examined after a digitalis treatment which caused the temporary disappearance of all the symptoms.

Soon after there was a second decompensation with symptoms superposed to the preceding. The examination of the blood on the 22-I2-24 refers to his second decompensation.

PATIENT 8: J.H., 44 years. Admitted to hospital for the first time in January I923.

Diagnosis: Pulmonary emphysema with successive cardiac decompensations.

No hereditary antecedent.

Personal antecedents: At I2 years of age generalised eczema; reappeared at I6 years then accompanied by attacks of asthma. In I9I9 had three successive influenzas with broncho-pulmonary phenomena. After these influenzas the respiration became difficult, especially at night or when in a lying position. From this time the face becomes congested and of a purple-blue colour under effort.

This patient presents a case of very special interest from the fact that he was examined before any phenomenon of cardiac decompensation. To make this case clearer, it is necessary to divide the study of the present illness into 7 periods:

I) before the cardiac decompensation, January 1923
2) during the first decompensation (18-7 to 1-8-23)
3) during the first digitalinis treatment (7-8-23 to 17-8)
4) during the second decompensation (31-8-23 to 20-9-23)
5) during the second recompensation (25-9-23 to 28-1-24)
6) during the third decompensation (30-1 to 5-2-24)
7) during the fourth decompensation (22-7-24 to 11-9-24)

First period: Cardiac Compensation.

The patient presents the characteristic aspect of severe emphysema. The face is purple red; without being really cyanotic, its aspect reminds us of the illness of Vaquez. Under effort the cyanosis becomes intense.

The thorax is rounded, particularly developed from front to back; the upper and lower clavicular cavities have disappeared, the thoracic expansion at the level of the arm-pits as at the level of the xyphoid process is of only 1 centimetre. The vital capacity is only 1500 cm3. The epigastric angle is very obtuse. The vocal vibrations have disappeared and the tympanism is intense on the whole pulmonary surface. Under auscultation the respiration is very muffled and, behind, the vesicular sound has almost disappeared at the two bases.

The heart shows a systolic indrawing at the apex. On percussion, the lefts edge reaches to the level of the nipple. The right edge reaches beyond the right parasternal line by two centimetres. The absolute dullness is greatly diminished in surface. There is nothing to note on auscultation. Under teleradiography the heart measures 15 centimetres in its transverse diameter.

The liver is large but not painful, neither spontaneously nor under pressure. It extends beyond the costal border by 4 fingers at the level of the mammillary line. The spleen is not palpable. The digestive, genito-urinary and nervous systems are normal.

This period includes numbers 1 and 2 of Table 12.

Second period: first decompensation.

The patient entered the hospital on July 16th.

He was obliged to cease work at the beginning of April; the attacks of suffocation ~~ss~~ return, the nights are without sleep on ~~a~~ account of the dyspnea, although, however, without any real attacks of asthma. The urine becomes scarce. After a digitalis treatment at home everything becomes right. He stops taking digitalis on July 8th.

On July 18th his blood flow is normal and his clinic examination on that day is similar to that of the first period.

From July 23rd there is a new attack of decompensation which I followed day by day. On July 24th oedema

appears on the legs and increases till the Ist of August. Albuminuria is abundant (2 grammes per thousand). There are neither cylinders nor cellular elements. The heart is triangular; under teleradiography it measures I7 centimetres in its transverse diameter. The liver is spontaneously painful and pulsatile. It measures 22 centimetres at the level of the crest. The abdomen is hard and distended. Finally purpuric spots soon appears over the tibias. The cyanosis is intense, even when resting. There are no moist ronchi in the lungs; the sibilances are abundant on the entire pulmonary surface.

This period extends from number 3 to number 9 of Table I2.

Third period: first recompensation.

Under digitalis treatment from 6-8-23, the patient's subjective symptoms improve rapidly when resting; the sleep soon becomes better, the attacks of dyspnoea become less frequent, to soon disappear; the peripheral oedemas are regularly resorbed, but there is still albumen without casts. The blood flow does not return to normal notwithstanding the administration of 4,5 milligrammes of digitaline. The liver, spontaneously painless, is painful upon pressure; the abdomen is still flatulent. This period extends from 7-8-23 to I7-8-23, the patient having shown signs of digitalis intoxication (cephalalgia, vomitings) on the I6-8-23.

Fourth period: second decompensation.

It is only a repetition of the second period. From the cessation of digitalis all the symptoms of decompensation reappear. This period extends from 3I-8-23 to 20-9-23.

Fifth period: second recompensation.

Much longer than the first recompensation it is also more complete through the disappearance of albumen and oedemas; the liver and heart return to their primary size, and the blood flow to the normal. The patient had been submitted to prolonged daily doses of digitaline, accompanied by theobromine and squill. This period extends from 25-9-23 to 28-I-24.

The sixth and seventh periods offer nothing of importance.

From the end of the action of digitalis, the signs of decompensation reappear (oedemas, albuminuria and usual subjective signs). It was not possible to follow up the examination because of an invading anasarca and the patient having left the hospital in the course of time.

In concluding it is well to note from now that the peripheral oedema has never appeared in this patient during the different decompensation till the blood flow diminished by 50 % at least. In the course of the first decompensation, it only made its appearance on 24-7-23; during the second on 20-9-23, and in the fourth on I-8-24 (see Table II).

Case 9: A.C. Normal subject

PATIENT IO: T.B., Pulmonary tuberculosis with extensive sclerotic lesions. Ordinary tuberculosis; at the two bases. The expectoration contains the Koch bacillus. The general condition is well maintained.

Case II L.D. Normal subject (myself)

PATIENT I2: G.V., 44 years. Admitted to hospital I-I-23.

Diagnosis: Arterio-sclerosis.

No hereditary antecedent. As personal antecedent had only acute bronchitis in I9I6. Since then chronic bronchitis with cough and morning expectorations, and attacks of nocturnal dyspnoea. The shortness of breath is intense under the least effort.

The face and nails appear cyanotic. There are no oedemas. The heart is slightly increased in size in all its diameters; the left ventricle is hypertrophied; under teleradiography it measures I6 centimetres in its transverse diameter. The sounds of the heart are dull and remote; there is no murmur.

At the level of the lungs no ronchi are heard, but a respiration extremely rough on all the thoracic surface. Under radiography an extensive bronchial sclerosis is observed.

PATIENT I3: H.H., 23 years. Circulatory insufficiency. Thyroid deficiency.

No hereditary antecedent. When 20 years of age he began to complain of general fatigue. From that time he has been subject to frequent syncopes. From that time he has also swelling of the feet in the evening, and the abdomen is generally distended after meals.

The patient, without now presenting any well-defined cardiac manifestations, nevertheless shows troubles of the circulation which one cannot, unfortunately, classify. He has acrocyanosis; the face is swollen and without energy; the shortness of breath is considerable under the least effort. The liver overlaps the false ribs by 4 centimetres and is painful under pressure. The basal metabolism was - 20 to - 26 % of the normal.

TABLE II

Circulatory Insufficiency. Arterial and Venous Blood.

Subject	No. of experiment	Date	Alveolar CO_2 %	Alveolar CO_2 mm Hg	Arterial Blood: CO_2 vol %	O_2 taken up vol %	O_2-Capacity vol %	Hb %	O_2-Saturation %	Alkaline Reserve at 40 mm of CO_2-pressure in vol % CO_2	pH	Venous Blood: CO_2 vol %	O_2 taken up vol %	O_2-Capacity vol %	Hb %	O_2-Saturation %	Alkaline Reserve at 40 mm of CO_2-pressure in vol % CO_2	pH	Expired Air Litres p. hour	CO_2 %	O_2 %	O_2 taken up %	R.Q.	Venous Tension CO_2 (mixed venous blood) %	Venous Tension CO_2 (mixed venous blood) mm Hg	Expired CO_2 p. minute cm^3	Blood Flow p.m. Litres.	Blood flow p. cycle c. cm^3	Pulse	Respiration p.m.
	1	7-XI-24			44.5	2.00	20.53	110	90.2	50.0	7.44	55.9	16.10	20.69	111	22.1	47	7.29											
II	1	16-XII-24			37.25	0.59	18.77	101	96.8	47.0	7.50																		
III	1	7-XI-23								52.0							48.5		~~442.5~~	~~3.36~~	~~17.00~~	~~4.09~~	~~.81~~	~~6.62~~	~~46.5~~	~~210~~	~~4.47~~	~~46~~	~~96~~	~~12~~
	2	8-XI-23	5.37	37.7															442.5	3.36	17.00	4.09	.81	6.62	46.5	210	4.47	46	96	12
	3	9-XI-23	5.14	35.8	49.0	0.32	17.08	92	98.1	52.0	7.40						48.5		457.0	3.33	16.98	4.12	.80	6.71	46.7	225	4.20	35	110	15
	4	13-XI-23	5.08	35.5	49.25	0.15	16.05	86	99.0	52.0	7.40	58.5	11.40	17.11	92	33.3	48.5	7.25												
IV	1	29-I-25					21.55	116		51.5				22.21	120		49													
V	1	26-XI-24			37.5	2.53	19.90	107	87.2	42.5	7.37	47.5	13.0	19.90	107	30.0	41.5	7.26											
VI	1	20-XI-22	4.82	34.6								57.2	13.05	20.30	109	35	46.5	7.27											
	2	14-XI-22	4.74	33.7	47.0	0.58	20.40	110	97.1	50.5	7.40			21.42	115		47.0													
	3	16-XII-22	4.76	32.9	46.9	0.85	20.20	109	95.8	51.0	7.41	61.7	15.0	21.15	114	29.0	47.0	7.22	575.0	2.44				6.35	43.9	210	3.90	46	85	20
	4	19-XII-22	5.09	35.2															582.5	2.37				6.54	45.3	205	3.90	46	85	20
VIII	1	10-1-23	9.39	65.8	68.5		(Normal Conditions)			60	7.26						60		384	4.10	16.32	4.78	.83	10.68	74.9	233	6.3	87	72	15
	2	12-1-23	8.91	63.0	69.5						7.28						60													
	3	30-7-23	7.65	52.4	59.0	2.93	21.79	112	86.5	52	7.30	73.5	10.4	25.60	138	59.3	46	7.09	388	3.58	16.43	4.75	.74	10.53	73.5	207	2.35	32	72	21
	4	31-7-23	7.14	50.0	59.0	2.36	22.0	119	99.2		7.32								395	3.72	16.37	4.79	.77	10.46	72.9	218	2.22	30	72	18.5
VII	1	5-XI-24				4.08	19.80	107	76.3	62		73.9	16.13	21.32	115	24.3	58	7.28	} 1st decompensation.											
	2	6-XI-24	7.05	50.3								77.5	15.5	21.66	117	28.4	58	7.26											
	3	24-XI-24					17.75	95		64		88.25	19.30	19.40	104	0.0	61.5	7.24	2d decompensation.										

IV THE ACID-BASE EQUILIBRIUM OF THE BLOOD IN CARDIAC PATIENTS WITHOUT VALVULAR LESIONS.

In Table 2 are collected some results found in patients presenting phenomena of cardiac decompensation without valvular lesions clinically disclosed.

Table 2 to be inserted here.....

Here we find characteristic phenominon of the circulatory stasis, that is to say the concentration in hoemoglobin of the venous blood at the same time as increase of pressure of the free carbonic acid. Indeed, the hoemoglobin calculated by the capacity of the blood in oxygen is always more abundant in the venous blood than in the arterial. We also see that the venous pH is regularly decreased and that the arterial blood is more alkaline than normally. The average of the arterial pH is 7,42 (the normal in the healthy subject is 7,35), and the average of the venous pH is 7,26 (the normal in the healthy subjest is from 7,32 to 7,33). The difference between the venous pH and the arterial pH which is normally from 0,02 to 0,03 (PETERS BARR and RULE (76), PARSONS (78), BIGWOOD (79)) is considerably exaggerated here (0,I6).

Finally, as in mitral stenosis, the dissociation curve of the venous blood falls in comparison to the curve of the arterial blood. Only one patient (case 5) shows a near resemblance between the arterial curve and the venous curve notwithstanding the considerable signs of cardiac decompensation. I have met this resemblance in numerous other cases of circulatory stasis, and we shall see another example of it in Table I2 (case

I, 28-II-24). We generally find in this contingency an arterial blood as rich in Hb as the venous blood, and it seems that in these cases we could admit that slowing of the circulation is uniformely distributed in the different parts of the organism, that is to say, it is no more pronounced at the level of the arms than in the other parts of the body.

There is another point to note, that is the absence of apparent oedema in cases 3 and 6, notwithstanding the passage of plasma into the tissues from the capillaries (as is proved by the concentration in Hb of their venous blood) and notwithstanding the considerable decrease of their blood-flow. We shall come back to this phenomenon later on (Table I2) when we study the blood-flow during decompensation; but it is useful to draw attention here to the fact that the stasis can exist manifestly without oedemas clinically disclosed.

The study of the oxyhoemoglobin saturation is also very interesting. One will observe that the arterial blood of all these patients is well saturated with oxygen, which proves that the cardiac decompensation had no action at the time on the oxygenation of the blood, that their cyanosis was only due to the circulatory stasis, and that their arterial alkalosis did not proceed from a primary need of oxygen in the lungs. The average of the arterial oxyhoemoglobin saturation in these 5 cases is 97,7 %.

As to the venous blood, it is considerably desaturated of oxygen, which had already been noticed on decompensated patients by C. LUNDSGAARD (80). The circula-

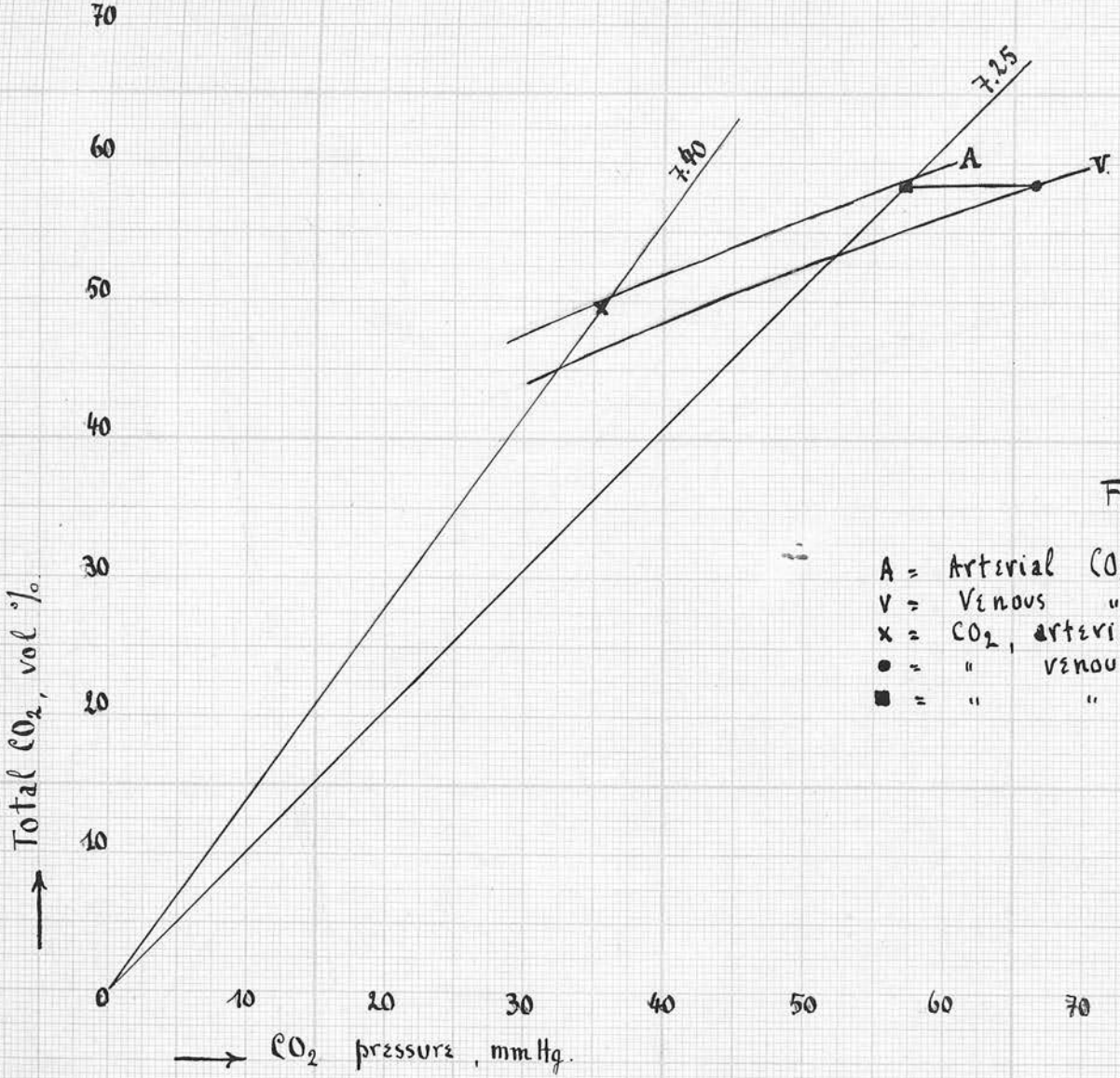


Fig III

A = Arterial CO_2-curve
V = Venous " "
x = CO_2, arterial blood, at alveolar CO_2-pressure
● = " venous blood
■ = " " " , corrected for O_2-desaturation

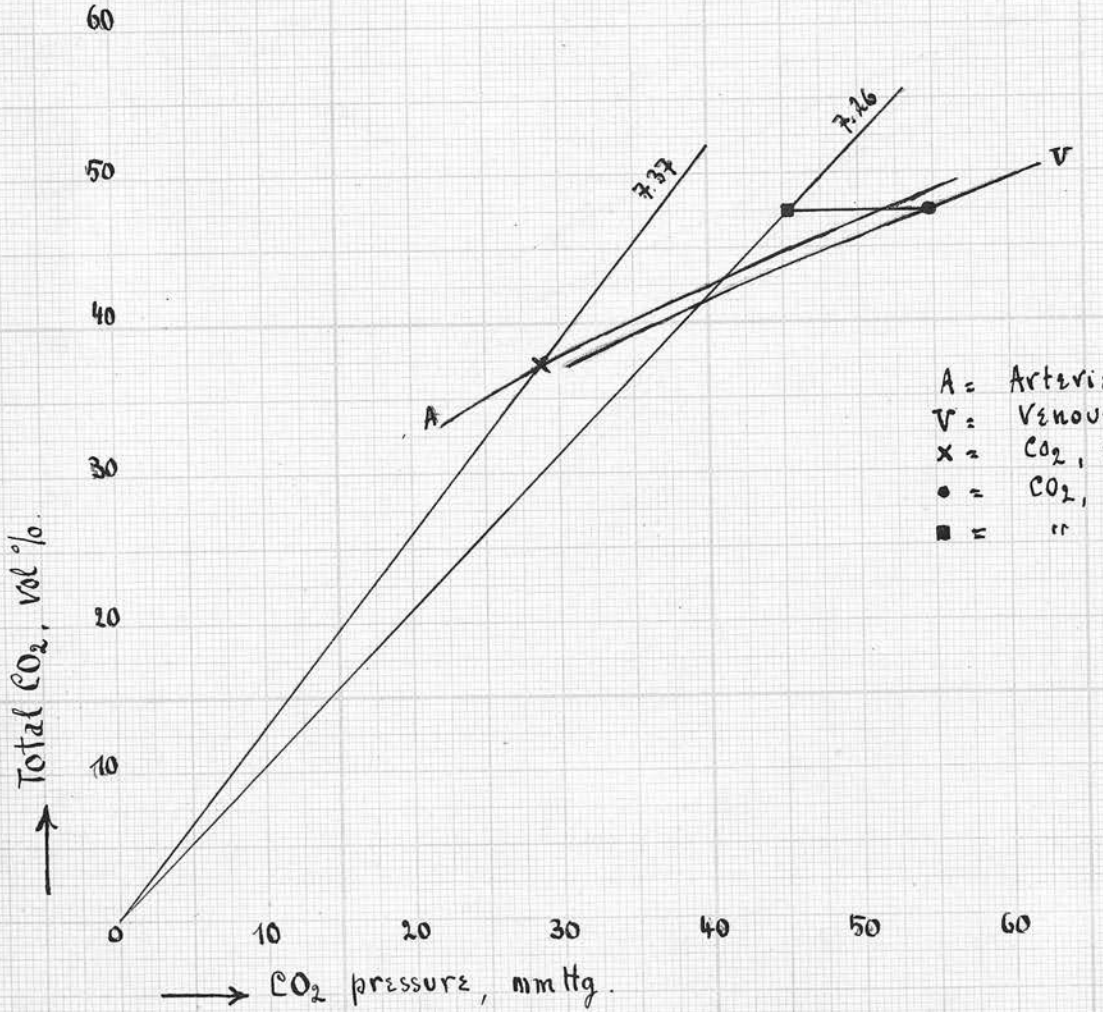


Fig IV

A = Arterial CO_2 curve
V = Venous " "
x = CO_2, arterial blood
● = CO_2, venous "
■ = " " " corrected for O_2 desaturation.

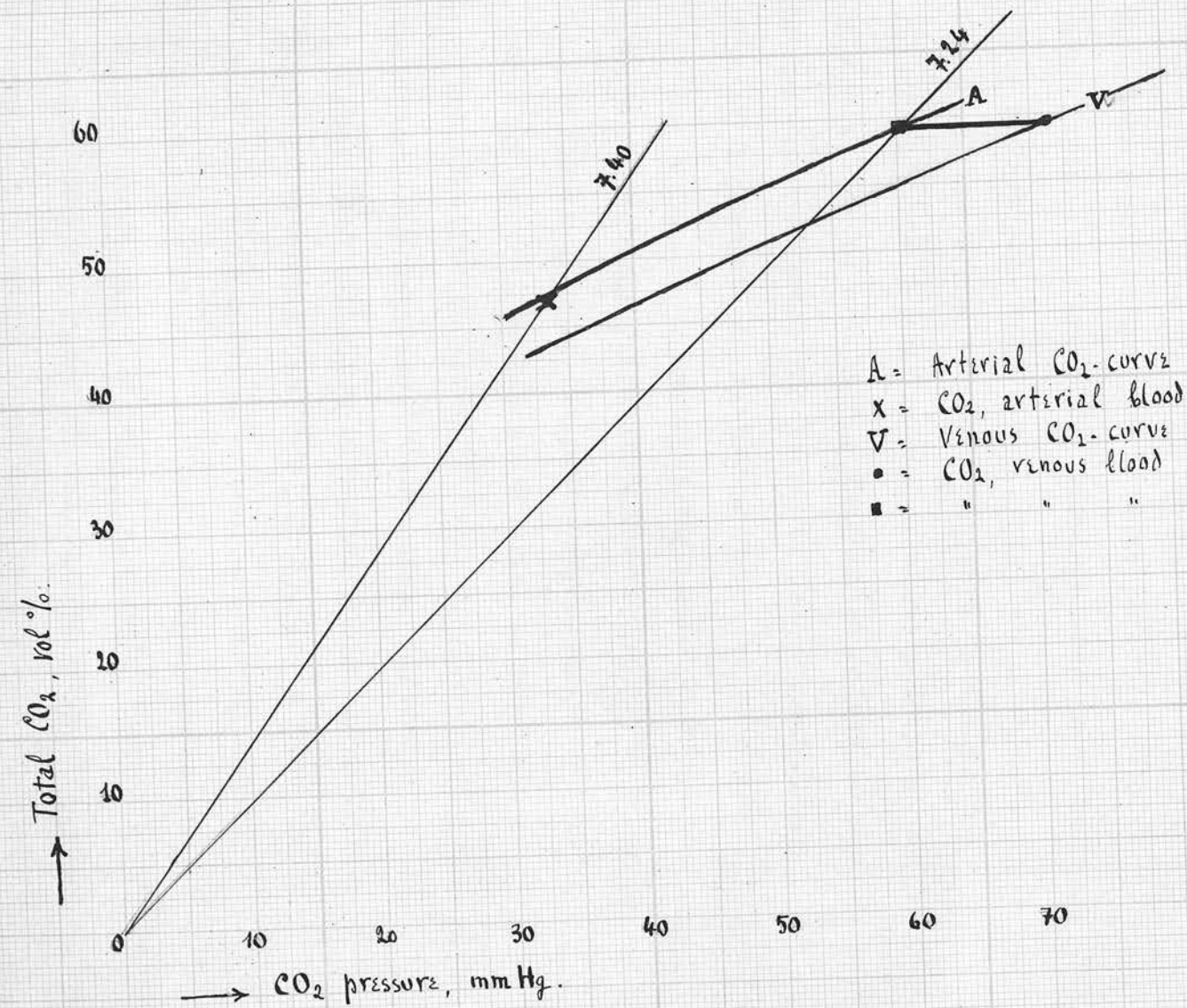


Fig V

A = Arterial CO_2-curve
X = CO_2, arterial blood, at alveolar CO_2 pressure
V = Venous CO_2-curve
● = CO_2, venous blood (mean)
■ = " " " " corrected for O_2-desaturation.

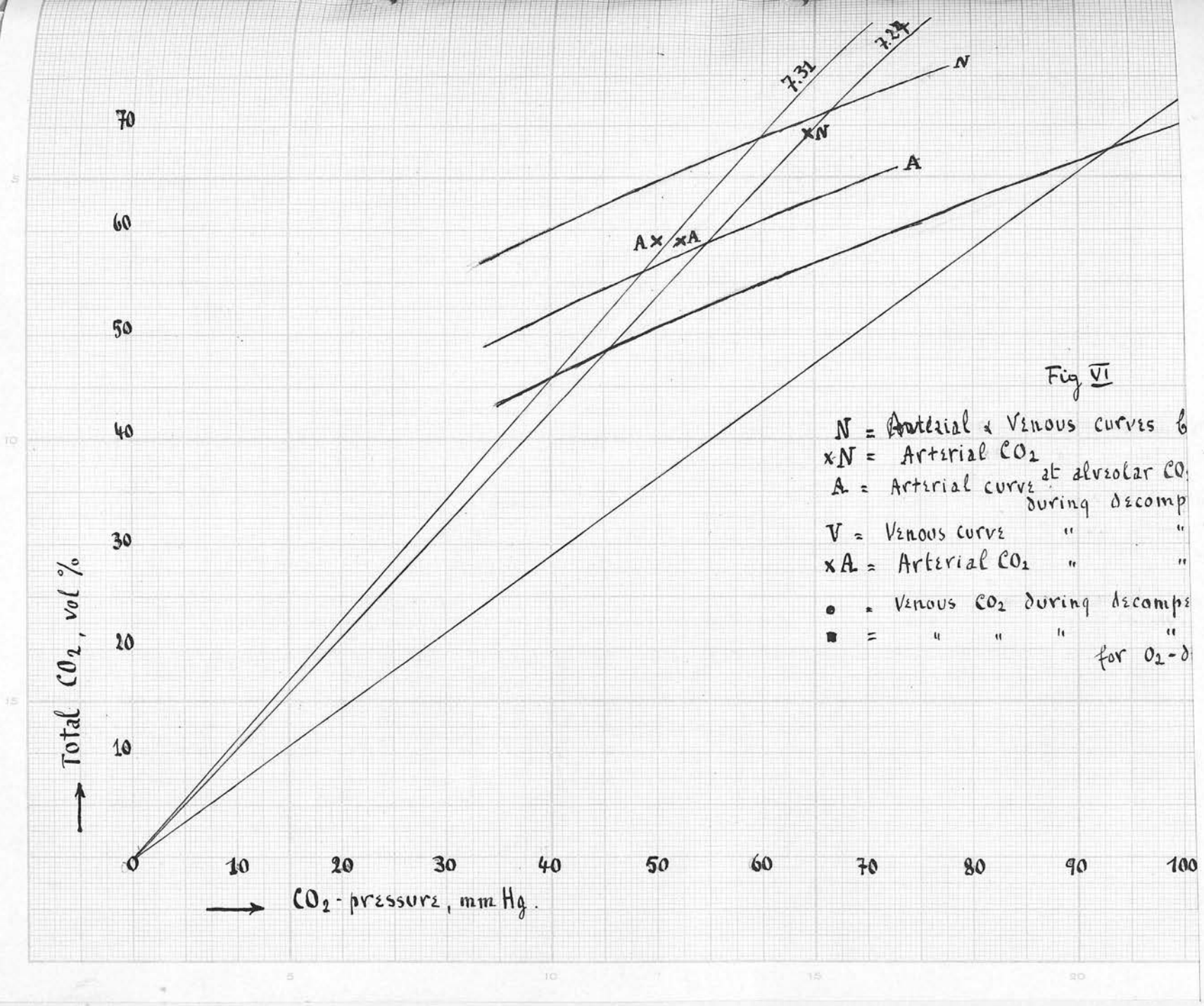
tory stasis easily explains this fact. The saturation of the venous blood, which is in healthy subjects from 50 to 60 % (C. LUNDSGAARD), is here of an average of 32 %.

The figures 3, 4 and 5 graphically sum up the observations of the patients 3, 5 and 6. The curve of the patients I and 2 will be found in the chapter treating of the therapeutics (figures 9 and I0).

Therefore we can say that, from the point of view of acid-base equilibrium, the cardiac patients without valvular lesions are in no way distinguished from the subjects with mitral stenosis.

But all the study of these patients is not confined to this. Table 3 puts in relief other phenomena which are worthy of attention. This table refers to two emphysematous patients, and it shows that we can find a curve of dissociation, either arterial or venous, higher than normally by decompensated cardiac subjects.

We know that emphysema is characterised by a retention of carbonic acid in the pulmonary alveoli followed secondarilly by an increase of arterial bicarbonate and of the alkaline reserve. It follows that in ordinary conditions the emphysematous possess a dissociation curve higher than the curve of normal subjects (SCOTT (8) MEAKINS and myself, not published). It is none the less true that this curve can also decrease during a cardiac decompensation, although the blood of these decompensated emphysematous cases is <u>positively</u> still richer in bicarbonate than the blood of healthy subjects. Besides, the curve of the venous blood can, as with the ordinary cardiacs, be lower than the curve of the arterial blood;


7.31
7.24
N
xN
A
Ax
xA
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
Total CO_2, vol %
CO_2 - pressure, mm Hg.
Fig VI
N = Arterial & Venous curves b
xN = Arterial CO_2
A = Arterial curve at alveolar CO
during decomp
V = Venous curve " "
xA = Arterial CO_2 " "
• = Venous CO_2 during decompe
■ = " " " "
for O_2 - d

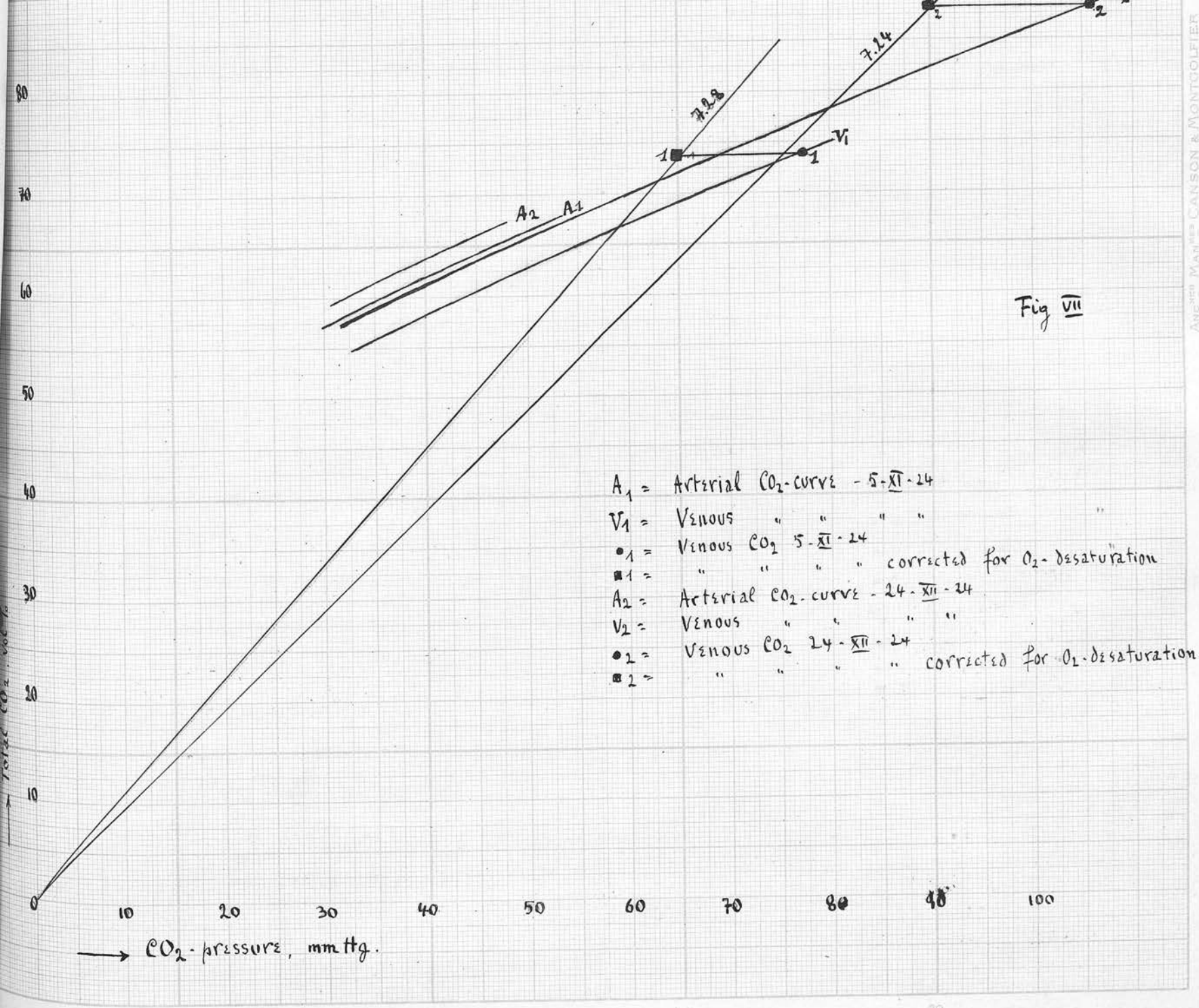


Fig VII

A_1 = Arterial CO_2-curve - 5-XI-24
V_1 = Venous " " " "
●1 = Venous CO_2 5-XI-24
■1 = " " " " corrected for O_2-desaturation
A_2 = Arterial CO_2-curve - 24-XII-24
V_2 = Venous " " " "
●2 = Venous CO_2 24-XII-24
■2 = " " " " corrected for O_2-desaturation.

the venous blood is also richer in Hb than the arterial blood.

It follows that one must be careful not to infer the absence of circulatory troubles from the fact that one finds in a patient a dissociation curve higher than normal.

We shall find in Table 3 and at figures 6 and 7 the summary of these observetions.

Figures 6 and 7 to be inserted here.

The first patient, very emphysematous, had by luck been examined in a perfect state of cardiac compensation. At this time the blood-flow was 6,3 litres per minute, and the curves of the venous and arterial blood were absolutely similar.

A considerable cardiac decompensation (see the clinical history) happened. The venous curve decreases and the arterial curve too, but the former more than the latter. We see in figure 6 that, in these conditions of intense decompensation, the venous curve of this patient corresponds to the normal curve of the blood of HALDANE, and that the curve of the arterial blood is still superior to it.

Confirmation of this fact is given by the examination of the blood of patient 7 (fig. 7), very emphysematous, also examined during two successive attacks of cardiac decompensation.

It follows from this that we must not base our calculations solely on one absolute value of the dissociation curve to decide upon the circulatory condition of a patient, but that we must construct the arterial curve as well as the venous, calculate the arterial pH

as well as the venous one. certain phenomena, as emphysema, can indeed hide a cardiac decompensation that the clinical observation, on account of the slowness with which the oedemas appear, often takes a long time to disclose.

CONCLUSION.

I) The stasis following cardiac affections without valvular lesions causes a fall of the alkaline reserve, accompanied by a decrease of the venous pH, by an increase of the arterial pH and by a concentration of the venous blood in hoemoglobin.

2) A single examination of venous blood cannot disclose a decrease of the alkaline reserve in the decompensated cardiac patients. The decrease can be hidden by a pulmonary element which has raised this curve before decompensation.

V) INFLUENEE OF LOCAL COLD BATHS ON THE CIRCULATION AND THE RESPIRATION.

Since the time that, struck by the close relations between the cold and the phenomena of shock various experimenters (especially WRIGHT and COLEBROOK) studied the action of the cold upon the circulation and the tissular respiration, the question has been neglected.

WRIGHT and COLEBROOK (8I), after having immersed animals in icy water found the venous blood poorer in bicarbonate than before the bath. They attributed the diminution of bicarbonate to the formation of lactic acid under the influence of asphyxia caused by the circulatory slowing.

As in these experiments the writers did not take into account the relations existing between the free carbonic acid and the combined carbonic acid and that the reaction of the arterial blood had not been considered, it seemed to me useful to again begin this study upon man, with technique much more delicate, and to reproduce by an ordinary physiological means a local stasis less severe than that caused by a tourniquet.

The cold was applied locally, by immersing the whole forearm in a bath, continually kept at 9 or I0 degrees Cent. The duration of the bath varied from 20 to 90 minutes. The symptoms during the bath are about the same in all cases. From the moment the arm was placed in water a general tickling, then a painful sensation of the elbow and the little finger; after four or five minutes insensibility appears sometimes preceded by a sensation of local heat and followed by complete

powerlessnes. After I5 to 20 minutes a sensation of electric shocks, is perceived, at first at the wrist at the level of the radial artery, then in the groove separating the external mass from the front mass of the muscles of the fore-arm, and finally in the entire fore-arm.

Objectively, the chronological phases are themselves fairly clear; at first a cyanosis in places, then rapidly after 3-4 minutes a redness appears at first with white areas, and then diffused. The superficial veins of the arm flatten and can become filiform. The goose flesh is then generalised; it soon disappears to exist only in the parts of the arm near the bath but not immersed (this latter zone can remain cyanotic during the complete duration of the bath). When the diffused redness has reached its height, the finger-nails of the other hand (not submitted to the cold) are cyanotic.

An oedema, slightly pronounced, but always perceptible and even measurable, appears after about half an hour. The intertendinous spaces of the back of the hand tend to be effaced and the fingers swell slightly. The blood of the arm under experiment is difficult to take without stasis, in consequence of the circulatory slowing and the weak intravascular blood pressure. Although flowing very slowly the blood has been, nevertheless, collected without stasis in all the experiments at present reported.

I) GAS OF THE VENOUS BLOOD.

MEAKINS and DAVIES (82) have shown that the fact of immersing a fore-arm in cold water would considerably

INFLUENCE of COLD LOCAL BATHS upon O_2-SATURATION of venous blood.

Subject IX Normal O_2-Saturation venous blood = 41 %
" O_2-Capacity " " = 18.0 vol %

Date	CO_2 vol %	O_2 taken up vol %	O_2-capacity. vol %	O_2-Saturation %	Conditions	
					Duration of bath. minutes	T° bath Degr. C.
15-4-24	55.8	4.50	19.40	51.0	3'	6-7°
11-4-24	51.0	8.18	19.80	58.6	10'	8°
14-4-24	57.0	7.77	20.38	61.3	20'	8°
23-4-24	59.0	5.61	18.68	70.0	40'	8°
18-4-24	57.5	3.60	17.60	79.5	40'	6-7°
18-4-24	56.5	3.60	19.19	81.2	60'	6-7°
23-4-24	54.5	2.73	19.23	85.8	65'	9°

TABLE IV

TABLE V

GASES of VENOUS BLOOD during cold local baths.

Subject	DATE	Conditions	CO_2 vol%	O_2 taken up vol%	O_2-capacity vol%	Hb %	O_2-Saturation %	Duration of bath. Minutes	Remarks.
IX.	28-2-24	normal	56.0	10.68	18.05	97	40.8		
	10-3-24	"	61.7	10.25	17.50	94	41.5		
	14-3-24	"			18.02	97			
	11-3-24	Cold bath	63.8	13.35	18.33	99	27.1	60'	other arm
	16-2-24	"	61.0	11.13	20.11	108	44.6	22'	
	21-2-24	"	54.0	5.30	20.54	111	74.2	55'	
	24-2-24	"	53.8	4.74	19.86	107	76.1	65'	
	27-2-24	"	53.0	5.12	19.87	107	74.4	80'	
X	23-11-23	normal	58.5	13.75	17.40	94	21.0		
	5-12-23	"	63.9	10.75	17.40	94	38.2		
	25-2-24	Cold bath	66.0	13.82	20.00	108	33.4	75'	other arm
	21-2-24	"		4.16	16.80	90	75.2	45'	
	22-2-24	"	60.3	2.40	20.04	108	88.0	65'	
VIII	26-3-24	normal		9.79	22.03	119	55.5		
	13-2-24	Cold bath		4.40	23.15	125	81.0	85'	
XI	13-3-24	normal			18.5	100			
	21-2-24	Cold bath	62.9	9.69	20.42	111	52.5	90'	other arm
	18-2-24	"	63.5	6.28	19.42	104	70.0	30'	

diminish the oxyhoemoglobin saturation of the blood taken from the elbow. After the immersion of a form-arm in ice, these writers have found a venous blood completely deprived of oxygen. However, we shall see in Table IV that another phenomenon rapidly appears if we leave the fore-arm in the cold water for a certain time, namely an increase of the oxyhoemoglobin saturation of the venous blood which may reach the arterial condition notwithstanding the considerable slowing of the circulation marked by the collapse of the superficial veins and the very weak intravascular pressure of the returning blood-flow.

We see in Table 4 that a certain relation also exists between the 02-saturation and the duration of the bath; it seems that the longer the bath (under the same conditions of temperature) the less the blood is desaturated of oxygen.

Another fact which will be met with in the different experiments regarding the action of the cold appears from Tables 4, 5, namely the concentration in hoemoglobin to which the blood of the arm is submitted on returning from the zones submitted to the cold. The hoemoglobin increases on an average of IO % during the cold bath.

In the venous blood of the left arm during the immersion of the right arm in cold water, or vice versa (heading: "opposite arm" in Tables 5, 6 and following) we see that the quantity of absorbed oxygen increases. We also see that the blood of the opposite arm also concentrates hoemoglobin as the blood submitted to the

TABLE VI

ALKALINE RESERVE, venous blood, during cold baths.

Subject	Date	Conditions	ALKALINE RESERVE at 40 mm Hg. in Vol% CO_2	Duration of bath Minutes	Remarks.
IX	28-12-23	normal	51.5		
	"	"	51.5		arterial blood
	10-3-24	"	51.5		
	29-2-24	"	51.5		
	"	"	51.5		arterial blood
	11-3-24	Cold bath	50	60'	other arm
	16-2-24	"	50	22'	
	26-2-24	"	48.5	55'	
	29-2-24	"	48.5	65'	
	27-2-24	"	46.5	80'	
X	29-11-23	normal	52.5		arterial blood
	6-12-23	"	52.5		"
	14-12-23	"	52.5		
	"	"	52.5		
	25-2-24	Cold bath	50.0	75'	Other arm
	22-2-24	"	48.5	65'	
VIII	26-3-24	normal	60		
	30-1-24	"	60		
	"	"	60		
	13-2-24	Cold bath	54.5	85'	
XI	13-3-24	normal	55		
	14-3-24	"	55		
	"	"	55		
	21-2-24	Cold bath	52	90'	Other arm
	18-2-24	"	54	30'	
III	22-5-24	normal	49		
	23-5-24	"	49		
	24-5-24	Cold bath	44	65'	

TABLE VII

ALVEOLAR CO_2 during cold baths.

Subject	Date	Conditions	Alveolar CO_2	
			%	mm Hg.
IX	14-12-23	normal	5.67	40.5
	"	Cold bath. 7 minutes	5.41	38.7
	"	" 40 "	5.06	36.2
X	21-2-24	normal	5.59	39.6
	"	Cold bath. 30 minutes	5.44	38.5
	25-2-24	normal	5.76	40.3
	"	Cold bath. 35 minutes	5.36	37.5
VIII	13-2-24	normal	8.64	59.9
	"	Cold bath. 30 minutes	7.78	53.9
XI	21-2-24	normal	5.92	42.2
	"	Cold bath. 90 minutes	5.27	37.4
III	20-5-24	normal	5.25	36.9
	"	Cold bath. 30 minutes	4.92	34.5

TABLE VIII.

Influence of local cold baths upon arterial blood.

Subject	Date	Conditions	Alveolar CO_2 mm Hg	ARTERIAL BLOOD		
				CO_2 vol%	O_2 Saturation %	ALKALINE RESERVE at 40 mm Hg. in CO_2, vol%.
IX	28-2-24	normal	38.6	50.3	98.0	51.5
	"	Cold bath. 75 minutes	35.1	48.4	97.0	50.0

cold.

2) ALKALINE RESERVE OF THE VENOUS BLOOD.

As we can see in Table 6 and at figure 8 for patient 9, the alkaline reserve of the venous blood of the arm under experiment decreases regularly. This phenomenon is also reproduced in the venous blood of the opposite arm although in a less degree for a local bath of the same duration.

3) ALVEOLAR AIR.

Three of the patients studied possess a normal alveolar air in ordinary conditions (40 mmHg). The fourth (case 8) was very emphysematous with an alveolar air rich in carbonic acid. Patient 3 is slightly below the average of healthy subjects.

From the beginning of the local cold bath, the alveolar air is impoverished in carbonic acid to considerable proportions in the five subjects studied.

Table 7 to be inserted here

4) ARTERIAL BLOOD.

with subject 9 the arterial blood was taken before and during the cold bath, the 02-saturation and the C02-content were determined, as well as the alkaline reserve. The alveolar air was collected shortly before the arterial puncture. We see in table 6 that, following the decrease of the alveolar carbonic acid, the arterial carbonic acid passes from 50,3 to 48,4 volumes % during the bath and that the 02-saturation remains perfect. The normal arterial alkaline reserve is exactly the same as that of the normal venous blood, but it slightly decreases during the cold bath.

TABLE IX

REACTION of THE URINE during COLD BATHS

Subject	Date	Conditions	REACTION URINES	CO_2 in the urines vol %	NNH₃	NNH₃ + N urea	$\frac{NNH_3}{N\ urea + NNH_3} \times 100$
IX	14-12-23	normal	acid	0	0.540	7.14	7.56
	"	Cold bath 70 minutes	alkaline	17	0.416	10.0	4.16
	17-12-23	normal	acid	0			
	"	Cold bath 110 minutes	alkaline	carbonates			
	23-4-24	normal	acid	0			
	"	Cold bath 50 minutes	alkaline	10%			
	18-4-24	normal	acid	0			
		Cold bath 40 minutes	alkaline	25			
X	22-2-24	normal	acid	0			
	"	Cold bath 70 minutes	alkaline	10			
XI	21-2-24	normal	acid	0			
	"	Cold bath 90 minutes	alkaline	68			
	"	1 hour after the end of the bath	"	33			

Table 8 inserted here.

5) URINE.

A similar decrease of the alveolar and arterial carbonic acid, and the alkaline reserve can be due to two causes, either to a non-gaseous acidosis, namely the penetration into the blood of acids stronger than H2CO3 or to a gaseous alkalosis, that is to say, to an exaggerated expulsion of carbonic acid by pulmonary ventilation. In the first case, the decrease of carbonic acid compensates that of bicarbonate; in the second, the alkaline reserve decreases to permit the ratio $\frac{H2CO3}{NAHCO3}$ to remain constant notwithstanding the decrease of the numerator.

In the first case, as we have seen, one of the means used by the organism is the passage of acids into the urine; in the second case, the urine becomes less acid than normally. Finally, when, in acidosis, the urinary ammonia increases, it decreases in alkalosis.

We see in Table 9 that, after the cold bath, the urine is alkaline and that it always contains bicarbonate, and with case 9 the relation $\frac{\text{Ammonia N}}{\text{Urea N}}$ falls considerably.

We are, therefore, in presence of a urinary alkalosis and this passage of bicarbonate into the urine is not due to a non-gaseous alkalosis, that is to say, to an increase of the denominator as after the ingestion of bicarbonate, since the alveolar air and the blood are poor in carbonic acid. We must, therefore, admit that it is due to an exaggerated expulsion of carbonic acid by overventilation.

TABLE X

EXPIRED AIR ; BLOOD FLOW during cold baths. (x)

Subject	Date	Conditions	Alveolar CO_2 mm Hg	Venous CO_2-pressure %	Venous CO_2-pressure mm Hg	CO_2, in volumes % corresponding to blood to CO_2-pressure: ARTERIAL	CO_2, in volumes % corresponding to blood to CO_2-pressure: VENOUS	Difference in vol % CO_2	EXPIRED AIR: Litres p. hour	EXPIRED AIR: CO_2 %	EXPIRED AIR: O_2 %	EXPIRED AIR: O_2 taken up, %	EXPIRED AIR: R.Q.	Expired CO_2 p. minute cm^3	BLOOD FLOW Liters p. minute	Blood Flow p. systole cm^3	Pulse	Respiration	Calories p. hour	DEAD SPACE for CO_2 cm^3
IX	13-12-23	normal	39.0	6.48	46.3	50.5	54.0	3.5	495.0	3.35	16.95	4.18	.794	250	7.14	105	68	14.8	91.0	220
	"	Cold bath 60 minutes	36.2	6.33	45.3	49.0	53.5	4.5	612.0	3.16	17.58	3.41	.917	294	6.50	98	66	22	95.0	177
	11-3-24	normal							452.0	2.99	17.29	3.82	.774	203			76	15	73	
	"	Cold bath. 10 minutes							490.0	3.10	17.21	3.89	.789	228			71	15.5	83	
	"	" " 40 "							500.0	3.01	17.31	3.79	.786	226			74	16	83	
X	25-2-24	normal	40.3	6.89	48.2	51.15	54.8	3.65	566.0	2.89	17.48	3.61	.792	244	6.7	67	98	16.6	88	283
	"	Cold bath 50 minutes	37.5	7.08	49.5	49.7	55.3	5.60	561.0	2.98	17.47	3.60	.820	248	4.4	41	106	16.5	88	255
VIII	13-2-24	normal	59.9	9.99	69.0	65.0	69.0	4.0	405	4.36				264	6.6	89	74	15.3		217
	"	Cold bath. 60 min.	53.9	9.68	67.0	62.2	68.0	5.8	422	4.07				256	4.4	63	70	17.0		199
	11-3-24	normal							382.5	4.58	15.69	5.43	.837	266			84	14.0	90	
	"	Cold bath. 10 min							427.5	4.78	15.65	5.42	.876	308			82	15.0	103	
	"	" 40 "							429.0	4.42	15.98	5.10	.860	284			76	15.8	97	
XI	18-3-24	normal							421.5	3.20	16.99	4.15	.760	202			89	11	75.4	
	"	Cold bath. 15 min							532.0	3.16	17.34	3.71	.843	251			88	16	87.0	
	24-3-24	normal							434.0	3.54	16.54	4.63	.758	228			90	11	84.9	
	"	Cold bath. 10 min							567.0	2.80	17.62	3.46	.800	233			92	19	84.8	

(x) The determination of the blood flow was started after the forearm had remained for a time in cold water (the column III)

Table 9 to be inserted here.

6) EXPIRED AIR. BLOOD-FLOW.

We shall see in the last chapter of this report that the fact of immersing a forearm in a bath at 45° can double the cardiac blood-flow. Table IO shows that the inverse effect is also produced, although to a less degree, and that a local cold bath slows the general circulation. The two determinations, in each case, were made on the same day, under the same conditions, at an interval of two hours. As in every circulatory slowing, we observe during the cold bath an exaggeration of the existing difference between the alveolar CO2 and the venous tension of this gas. The decrease of the systolic delivery is principally responsible for that of the blood-flow; the ventilation is generally increased; finally the dead space of the respiratory system calculated by means of the DOUGLAS and HALDANE's (85) formula:

Dead space = Vol. per respiration - Vol.p.resp. $\times \frac{CO2 \text{ exhaled}}{\text{Alveolar } CO2}$

is diminished during the cold bath, so that the effective ventilation is still increased. The following chapter will treat of the modifications of this dead space and of the effective ventilation during the cardiac decompensation.

As in forced pulmonary ventilation, the respiratory quotient increases, and the metabolism. These same modifications of the metabolism and R.Q. were observed a long time ago during general cold baths (LOEWY,I890; SPECK,I892; JOHANNSSON,I896; RUBNER, I902 (84)).

TABLE XI

ARTERIAL & VENOUS pH, during cold bath.

1. Subject	2. Conditions	3. ARTERIAL pH	4. VENOUS pH (mixed venous) blood	5. Difference between 3 & 4	6. VENOUS pH (arm)	7. Difference between 3 & 6	Remarks.
IX	normal	7.36	7.31	0.05	7.32	0.04	
	Cold bath	7.39	7.32	0.07	7.26	0.13	
	"				7.26	0.13	other arm
X	normal	7.37	7.32	0.05	7.33	0.04	
	Cold bath	7.39	7.32	0.07	7.19	0.20	
	"				7.22	0.17	other arm
VIII	normal	7.28	7.23	0.05			
	Cold bath	7.31	7.24	0.07			
XI	Cold bath				7.29		
	"				7.29		other arm.

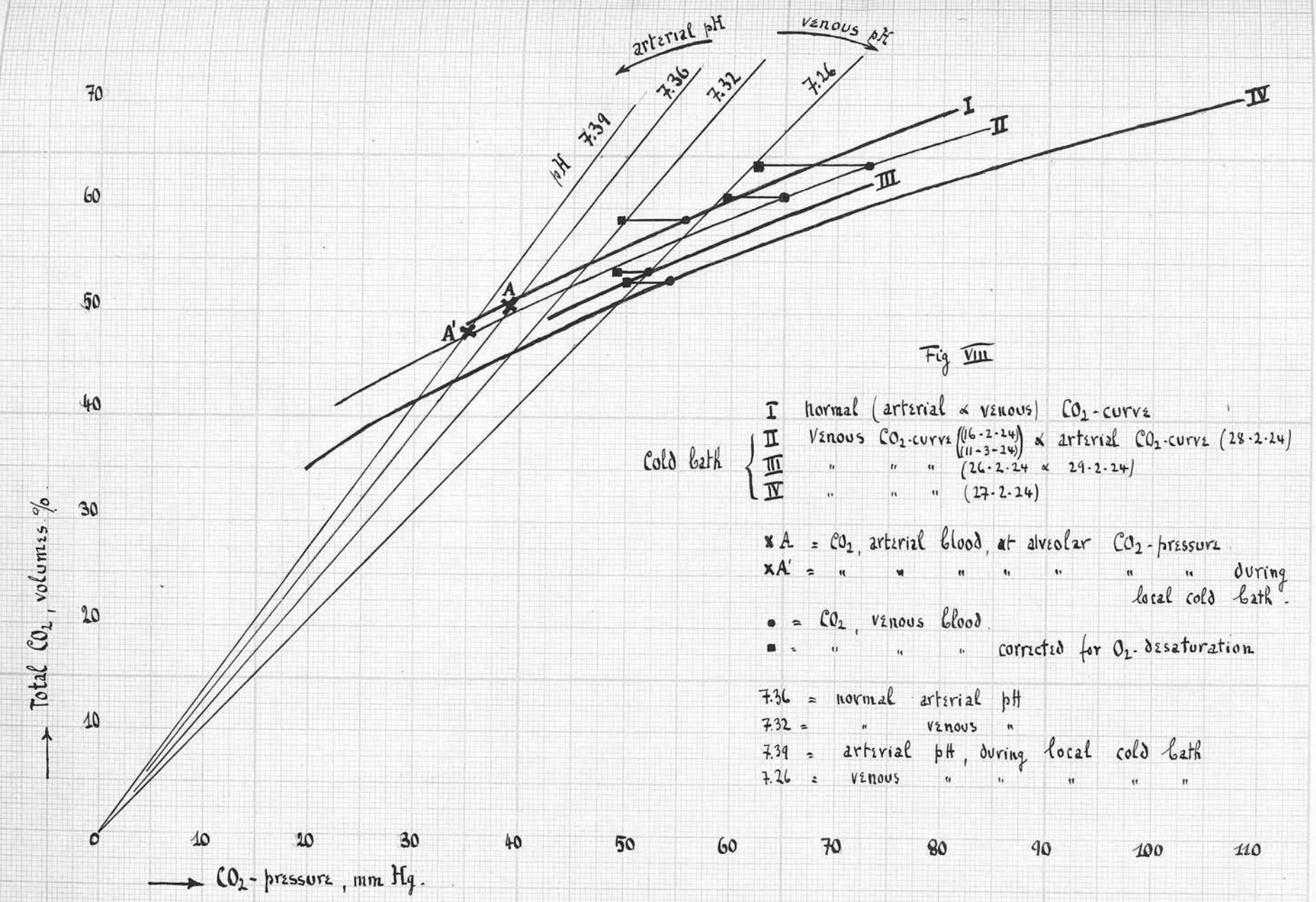


Fig VIII

Cold bath
- I Normal (arterial & venous) CO_2-curve
- II Venous CO_2-curve ((16-2-24) / (11-3-24)) & arterial CO_2-curve (28-2-24)
- III " " " (26-2-24 & 29-2-24)
- IV " " " (27-2-24)

× A = CO_2, arterial blood, at alveolar CO_2-pressure
× A' = " " " " " " " during local cold bath.
• = CO_2, venous blood
■ = " " " corrected for O_2-desaturation

7.36 = normal arterial pH
7.32 = " venous "
7.39 = arterial pH, during local cold bath
7.26 = venous " " " " "

7) pH.

Table II clearly shows the increase of the arterial pH during local cold baths, the decreases of the venous pH in the arm submitted to the bath as also in the opposite arm and in the mixed venous blood.

Figure 8 graphically sums up the observation of the subject 9. There we see the successive decreases of the alkaline reserve in the blood of the arm under experiment, a similar decrease, although of less intensity, in the blood of the opposite arm, the decrease of the arterial carbonic acid opposite the diminution of the alveolar carbonic acid, and finally the secondary fall of the dissociation curve of the arterial blood.

Figure 8 to be inserted here.

DISCUSSION.

As WRIGHT and COLEBROOK saw it, the cold bath diminishes the quantity of bicarbonate of the venous blood. The venous blood is in an acidotic state generally very pronounced. WRIGHT and COLEBROOK attribute, as we have seen, this acidosis to the passage into the blood of lactic acid of which the formation would be due to asphyxia itself caused by the circulatory slowing. It is difficult to admit this hypothesis. Indeed, DAUTREBANDE, DAVIES and MEAKINS have not been able to put in evidence an excess of lactic acid in the blood completely desaturated of oxygen of a forearm submitted to a severe stasis of 40 to 50 minutes. On the other hand, the venous blood of the arm submitted to the cold, and of which the oxyhoemoglobin saturation is far from being exhausted, sees its alkaline reserve

decrease in its turn. Finally, if it is a non-gaseous acidosis due to the lactic acid, we hardly understand why this lactic acid does not pass into the general circulation. As a matter of fact the arterial blood is more alkaline than normally, to such an extent that the urine becomes alkaline and contains bicarbonate.

It is more probable that the venous acidosis of the cold bath is of the same order as the acidosis of the stasis caused by a tourniquet or by a disease of the circulatory system. All the elements of this particular acidosis are indeed found during the cold bath: I) Concentration in hoemoglobin, 2) increase of the pressure of carbonic acid in the blood of the arm under experiment as well as in the opposite arm. The circulatory slowing in the opposite arm is marked besides by the presence of cyanosis, a cyanosis which contrasts strangely with the brilliant red tint of the arm under experiment. This circulatory slowing in the opposite arm is in all probability of reflex origin.

As to the nature of the arterial alkalosis, it has been sufficiently studied in the course of this chapter. It cannot be a question of a non-gaseous alkalosis since the pressure of the alveolar carbonic acid diminishes, that the respiratory quotient increases, that the ventilation is always increased, and that the alkaline reserve decreases in the arterial blood.

The overventilation which produces this arterial gaseous alkalosis by expulsion of carbonic acid is not due to pain: this pain only exists during the first two or three minutes of the experiment; besides, it

may be entirely absent. Moreover, in order to avoid this pain the temperature of the bath was never lowered under 8 - 9 degrees. The exaggerated expulsion of CO2 is rather due to the circulatory slowing in the medulla oblongata which causes an accumulation of H ions to which the respiratory centre responds by overventilation. This is after all the same phenomenon as that which is produced in the decompensated cardiac patients. It is nevertheless to be noted that the circulatory slowing does not reach all parts of the body to the same extent since the urine is alkaline, which leaves us to suppose that the circulation in the kidneys was not diminished.

At present I have no definite explanation to give for the inability of the tissues to absorb the oxygen of the blood. The same phenomenon was observed, entirely independent of myself, by GOLDSMITH and LIGHT, at the moment when these experiments ended. The tissues entirely lack the power to absorb the oxygen of the arterial blood; indeed with the arm in cold water, this inability persists when the venous circulation is secondarily stopped by a very tightened tourniquet. This lack of power in the tissues seems to become gradually greater as the bath is prolonged; indeed from the first minutes the skin is bright red whilst the oxyhoemoglobin saturation of the venous blood continues to rise as the bath is prolonged.

CONCLUSIONS.

I) We find in the course of the cold baths localised to a fore-arm most of the characters of the

experimental or clinical circulatory slowing, namely the concentration of the blood in hoemoglobin along with an increase of pressure of the free carbonic acid and a decrease of the alkaline reserve, in the blood of the arm under experiment as well as in the blood of the opposite arm.

2) During the local baths the arterial blood is in a condition of gaseous alkalosis, marked by an increased pulmonary ventilation with increase of the R.Q. and by the decrease of the alveolar CO2, and reduction of the arterial bicarbonate and also by the emission of alkaline urine.

3) From three experiments with different subjects, it follows that during the cold local baths the blood flow diminishes, which explains the arterial alkalosis: the circulatory slowing causes an accumulation of carbonic acid in the medulla oblongata to which the respiratory centre responds by overventilation.

4) The tissues submitted to the cold become incapable of absorbing oxygen; the venous blood which returns from them may, in time, be as completely saturated with oxygen as the arterial blood.

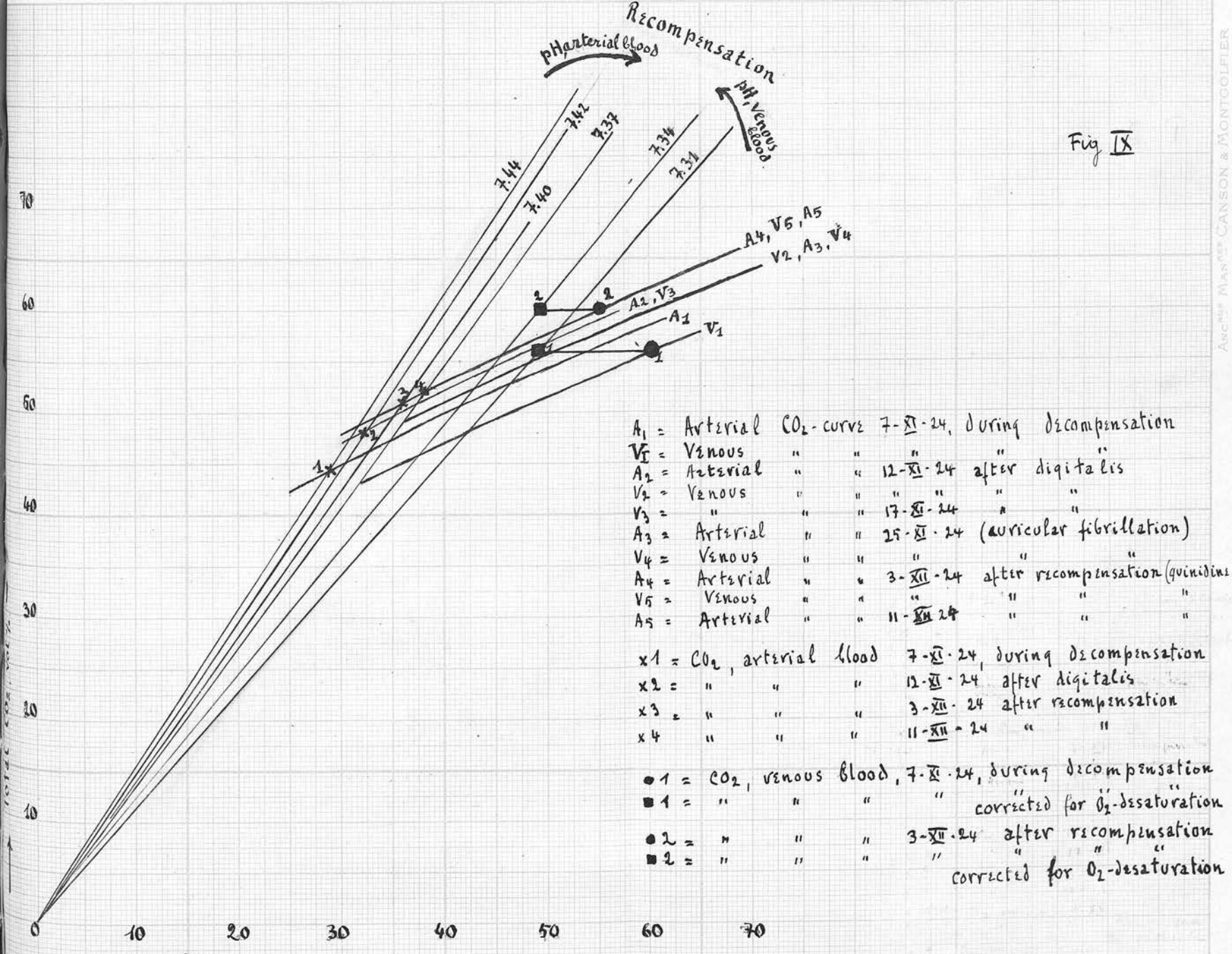


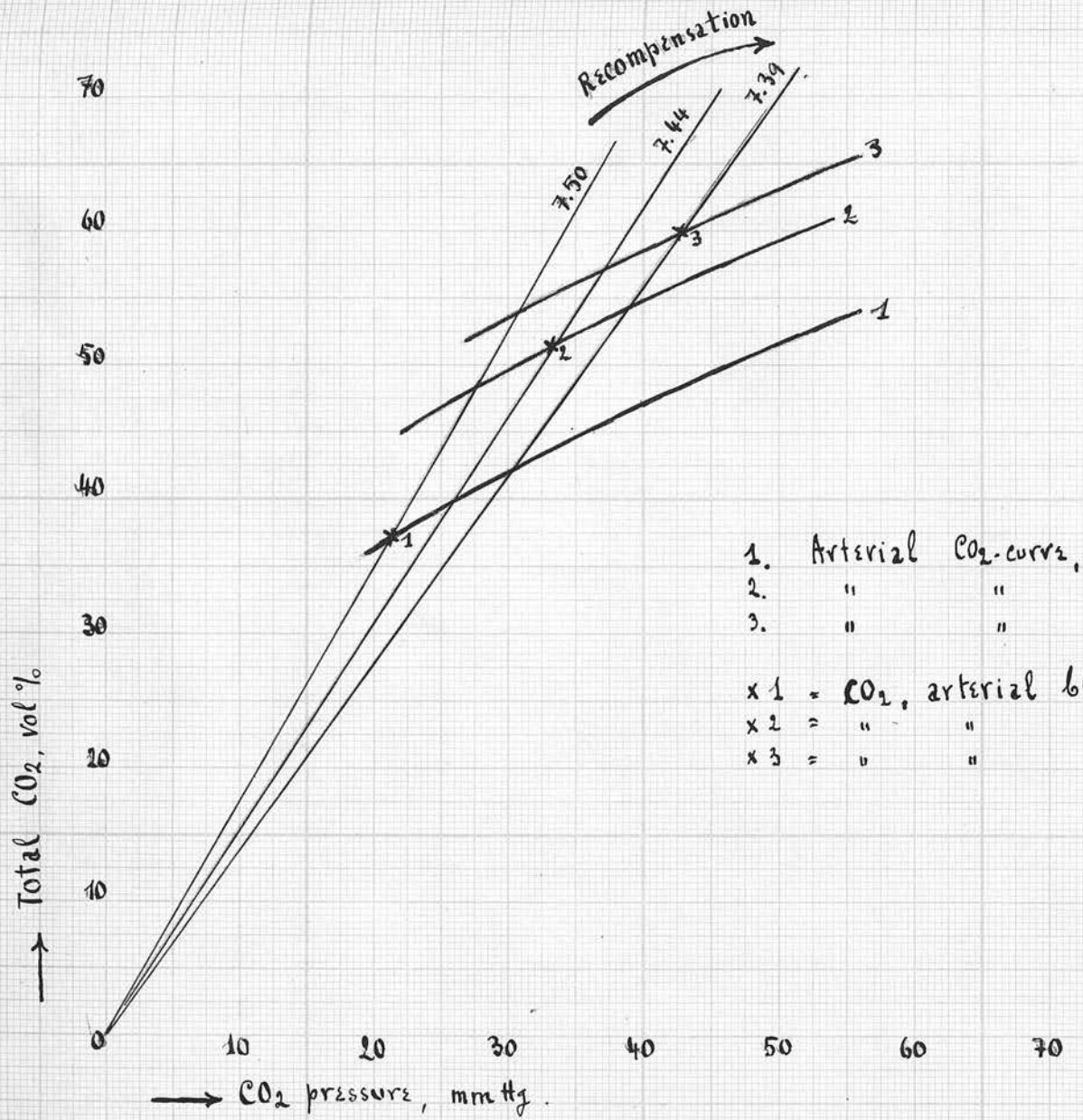
Fig IX

A1 = Arterial CO_2-curve 7-XI-24, during decompensation
V1 = Venous " " " " "
A2 = Arterial " " 12-XI-24 after digitalis
V2 = Venous " " " " " "
V3 = " " " 17-XI-24 " "
A3 = Arterial " " 25-XI-24 (auricular fibrillation)
V4 = Venous " " " " "
A4 = Arterial " " 3-XII-24 after recompensation (quinidine)
V5 = Venous " " " " " "
A5 = Arterial " " 11-XII 24 " " "

x1 = CO_2, arterial blood 7-XI-24, during decompensation
x2 = " " " 12-XI-24 after digitalis
x3 = " " " 3-XII-24 after recompensation
x4 " " " 11-XII-24 " "

● 1 = CO_2, venous blood, 7-XI-24, during decompensation
■ 1 = " " " " corrected for O_2-desaturation
● 2 = " " " 3-XII-24 after recompensation
■ 2 = " " " " corrected for O_2-desaturation

Fig X



1. Arterial CO_2-curve, 16-XII-24, During decompensation
2. " " 15-1-25 " recompensation
3. " " 24-2-25 " " "

x 1 = CO_2, arterial blood 16-XII-24, decompensation
x 2 = " " " 15-1-25, recompensation
x 3 = " " " 24-2-25, "

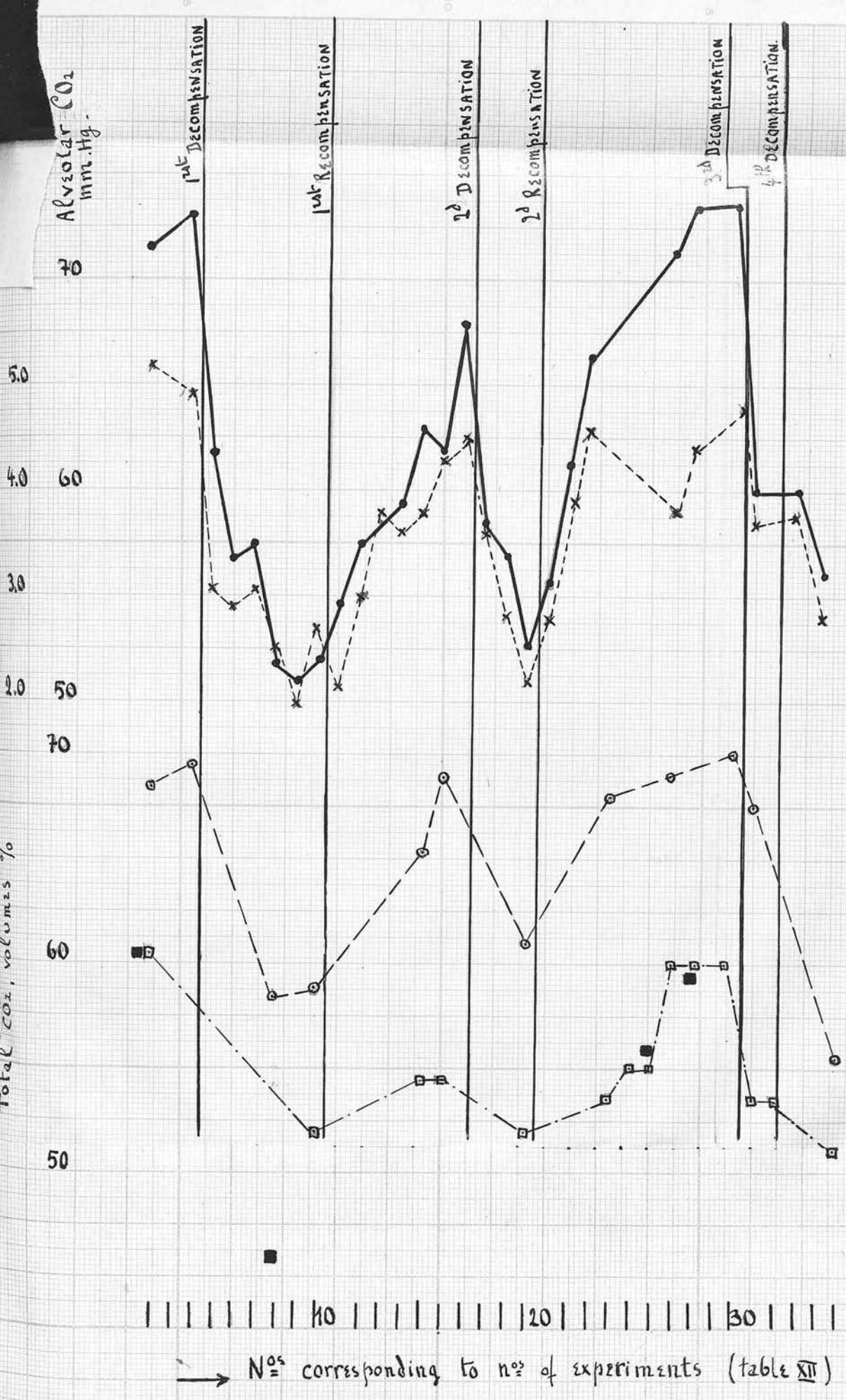


Fig XI

Blood flow, Liters per minute

Alveolar CO_2, mm Hg.

CO_2, arterial blood.

Arterial CO_2-curve, at 40 mm Hg of CO_2-pressure

Venous " " " " " " "

VI

THE TREATMENT OF CARDIAC DISEASES AND ITS INFLUENCE UPON THE ACID-BASE EQUILIBRIUM OF THE BLOOD.

If it is true tha the circulatory stasis is the cause of all the modifications of the acid-base equilibrium of the blood that we have just studied (arterial alkalosis, venous acidosis, decrease of the alkaline reserve) it is evident that with subjects suffering from cardiac decompensation, an appropriate treatment must put everything in order.

Table I2 and figures 9, I0 and II show it.

Subject I is interesting from numerous points of view. We see that in the course of a first digitalis treatment the arterial curve rises, followed by the curve of the venous blood which joins it after a certain delay (experiment 3). The arterial alkalosis and venous acidosis decrease. Then, at the moment of the appearance of the auricular fibrillation, in the absence of any treatment the curves decrease again and are superposed (28-II-24). Finally, a quinidine treatment definitely raises the two curves which are supersosed.

Figure 9 permits us to notice the inverse route followed during the recompensation by the arterial pH which decreases and the venous pH which increases; they tend therefore to draw nearer as the condition of the circulation improves.

We shall also notice the oscillation of the oxyhoemoglobin saturation of the venous blood: the better the compensation, the more is this blood saturated with oxygen. We see the saturation of the venous blood decrease again when the auricular fibrillation

appears (28-II). Table I2 and figure 9 also permit to follow the progressive increase of the arterial CO2 during the recompensation. But, undoubtedly, the most important point is the way in which the value of the hoemoglobin, arterial and venous, acts. As compensation returns and the curve increases, the hoemoglobin of the blood decreases. This is easily explained by the return into the general circulation of the plasma which had originally passed into tissues and this seems to clearly indicate that, during the cardiac decompensation, the volume of circulating blood is diminished. This, in short, explains that the curve of the arterial blood can be decreased during the cardiac decompensation, as well as the venous curve.

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" "

With subject 2, it was not possible to follow regularly the modifications of the venous blood which could only be collected once without stasis, but the study of the arterial blood is also instructive. The phenomena studied in subject I are repeated: in the course of the recompensation the alkalosis disappears, the dissociation curve rises again, and the rate of the hoemoglobin diminishes progressively. This last fact confirms what has been said concerning subject I: it seems it can only be explained by the reappearance of previously extravasated liquid in the circulating blood.

Figure I0 brings a new argument in favour of the proposition enunciated in Chapter I concerning the

emphysematous cases. Here, the circulatory stasis has considerably lowered the curve to the extent of causing the characteristic of the blood of the emphysematous to disappear, namely, the increase of the alkaline reserve. During the recompensation this alkaline reserve increases much beyond the normal, which the clinical signs of emphysema could enable us to foresee.

"

" "

The case 8 is of very special interest through the fact that the modifications of the acid-base equilibrium during different decompensations and recompensations were controlled by the blood-flow and the alveolar air. Figure II sums up in a striking way all the physiopathological history of this patient. It will be good, in order to follow this subject to advantage, to refer to the summary of the clinical observation.

Figure II clearly shows the successive and parallel oscillations of the alveolar carbonic acid, of the total arterial carbonic acid, of the blood-flow and of the alkaline reserve; one can thus notice the clinical value of the biological control given by the examination of the blood during cardiac decompensation.

This case resembles all the physio-pathological aspects of the cardiac decompensation. However, it will be well to repeat some remarks: at first we can see that during cardiac decompensation the alveolar carbonic decreases considerably, although, in consequence of the emphysema, it still remains above the normal of healthy subjects. It is the same with the curve of the arterial blood, the arterial CO_2 and the venous CO_2.

The blood-flow decreases regularly during the different decompensations. An examination of Table I2 puts some interesting points in relief:

I) The difference which exists between the pressure of the arterial carbonic acid and that of the carbonic acid of the mixed venous blood increases more and more, which corresponds, on the one hand, to the decrease of the alveolar CO2, and, on the other hand, to the accumulation at the level of the tissues, of carbonic acid through the circulatory slowing. The difference between the arterial and venous contents of carbonic acid, which was 3,7 when the blood-flow was normal can reach 9,8 when the blood-flow falls to 2,2 litres per minute (3I-7-23).

2) During the recompensation, this difference decreases progressively: the alveolar CO2 reaccumulates, and, as the stasis is removed the blood of the capillaries no longer stores as much carbonic acid, that which diminishes the pressure of this gas in the mixed venous blood.

Nevertheless, the first recompensation offers a peculiarity upon which we must enlarge. We see in Table I2 and at figure II that, under the influence of digitalis the alveolar air and the arterial CO2 return exactly to the starting point, but that I) the curve of the arterial blood only rises very little; 2) notwithstanding the considerable doses of medicine administered the blood-flow does not regain its original level; 3) that, in the same way, the difference between the quantity of arterial CO2 and of the CO2 of

the mixed venous blood remins at 5,6 instead of descending again to the normal (3,7).

The clinical history, teaches us that at this moment, notwithstanding the disappearance of the peripherab oedemas an albuminuria without cylinduria always continued abundant and the liver remained large and painful.

It seems that from the whole of these findings, we may discover the phenomenon which has given rise to these anomalies.

A) Under the influence of digitalis, the respiratory centre being better irrigated, has enabled the reaccumulation of carbonic acid in the alveolar air and the arterial blood.

B) Although it had disappeared from the extremities, the stasis has continued in the abdomen; through this a part of the mixed venous blood returned from zones where the circulation was still deficient, and it is clear that, from this fact, the pressure of the carbonic acid in the blood could not completely return to the normal, and that, notwithstanding the digitalis, it remained higher than before the decompensation. This explain why, although the pressure of the alveolar carbonic acid has returned to its starting point, there is still, instead of 3,7, a difference of 5,6 volumes% of CO2 between the arterial blood and the mixed venous blood.

C) This also permits us to understand why the dissociation curve of the arterial blood rises only insufficiently (see fig.II). Indeed, at the level of

the stasis the bicarbonate does not succeed in repassing from the tissues towards the blood as in the peripheral zones where the stasis is removed and where the oedemas are resorbed.

D) An experiment, which is part of another group of researches, confirms the probability of this explanation; in placing hot sand or hot compresses on the abdomen of this patient in order to accelerate the circulation at this level one saw the dissociation curve of the arterial blood immediately rise up to its normal level and urine was, from the first minute of this hot application, free from albumen.

From the whole of these facts we can conclude that during this first digitalis treatment the circulation was in a certain way hindered, certain zones of the circulatory system remaining in stasis near other vascular parts which had retaken their normal circulatory course.

Besides, during the second recompensation this phenomenon did not reappear again. At the same time as the alvéolar and arterial CO2 reaccumulated, the arterial dissociation curve regained its original level, the difference between the arterial CO2 and the CO2 of the mixed venous blood became normal again and blood-flow retook its original value. The albuminuria and the hepatic congestion had disappeared.

3) Another fact to be noted is the slight apparent change undergone by the quantity of expired air during the decompensation. I have met the same phenomenon in other emphysematous patients with decompen-

sated hearts. This is apparently due to the rigidity of their thorax which does not permit either the entry into or the issue from the chest of large quantities of air. The thoracic expansion of this subject was only I centimetre and his vital capacity only I500 cm3. We see besides that in the course of this long observation the arterial pH is far from increasing in considerable proportions. From 7,27, which it is during the periods of compensation, it only reaches 7,3I during the different decompensations (average figures).

This does not mean that the emphysematous cannot overventilate, nor increase their arterial pH considerably. In this case we observe that the thoracic expansion is normal and that the thorax is far from being rigid. Subject 2, which is in this latter category, had a thoracic espansion of 4 centimetres.

Nevertheless, there is in subject 8 a real increase of pulmonary ventilation; if we calculate the dead space of the respiratory system by the DOUGLAS and HALDANE's formula, we notice that this dead space generally diminishes during decompensation, in such proportions that the effective pulmonary ventilation in unit of time is increased. By effective pulmonary ventilation one means the quantity of air of each respiration from which we have substracted the dead space. To obtain the effective pulmonary ventilation per minute, it is, therefore, sufficient to multiply the figure thus obtained by the number of respirations per minute.

If we calculate the effective pulmonary ventila-

tion up to the end of the second recompensation (7-II-23) in order to have figures referring to one short period, we find that the effective pulmonary ventilation is I80 litres per hour during the normal period, and the period of recompensation, and 2I6 litres per hour during the two periods of decompensation.

In concluding this chapter, it is well to notice that I) during the successive periods of compensation and decompensation the pulse remains constant and that the decrease of the blood-flow is solely attributable to the decrease of the systolic flow; 2) that the clinical signs of oedema only appear during the decompensation at the moment when the blood-flow has already diminished by 50 %.

CONCLUSION.

I) The treatment of cardiac patients causes the characteristic troubles of the acid-base equilibrium promoted by the blood stasis either to disappear or diminish: concentration of the blood in hoemoglobin, arterial alkalosis and venous acidosis.

The results of this treatment prove that the curve of the arterial blood can fall during the decompensation in the same way as the curve of the venous blood, although often to a less degree.

The concentration of the arterial blood during the decompensation and its dilution during the recompensation seem to indicate that, in the first case, the volume of the circulating blood is diminished.

VII

INFLUENCE OF LOCAL HOT BATHS

LOCAL ACTION; GENERAL ACTION.

MEAKINS and DAVIES have shown that if we place a fore-arm in a bath at 45° C, the blood which was returning from the immersed parts kept, on account of the increase of the circulation, the oxhoemoglobin saturation and the CO2 contents of the arterial blood.

Later on, MEAKINS, FETTER and myself ascertained the same phenomenon in patients suffering from mitral stenosis. Under the action of baths of the fore-arm at 45° the blood of the arm again became arterial; moreover, the dissociation curve of this blood, previously lowered by stasis, came again exactly to the height of the arterial curve, which proves indirectly that the original fall of the alkaline reserve of the venous blood was certainly due to stasis.

I have again made these exmeriments from a more general point of view with different patients, whose history has been reported in the course of this study.

These different experiments are set out in Tables I3, I4, I5, I6 and I7.

I)LOCAL ACTION OF LOCAL HOT BATHS.

In this respect these new experiments add nothing to what MEAKINS, FETTER and myself had ascertained in patients suffering from mitral stenosis. During these baths the venous blood again becomes arterial and its curve rises (subjects 6 and I3 Table I3). Its pH also increases considerably.

TABLE XIII

BLOOD-GASES during warm local baths.

Subject	Date	Conditions	ALKALINE RESERVE at 40 mm Arterial blood - in vol % CO_2	VENOUS BLOOD					
				CO_2 vol %	O_2 taken up vol %	O_2 capacity vol %	O_2-Saturation %	ALKALINE RESERVE at 40 mm in vol % CO_2	pH
VI	4.12.22	normal	51.0	57.2	13.05	20.30	35	47.5	7.27
		1 forearm at 45°		46.5	1.23	20.80	94	51.0	7.42
	26.12.22	normal		61.7	15.0	21.15	29	47.5	7.22
		Blood of the left arm during a bath of the right arm (45°)		53.4	6.67	21.13	68.4	51.5	7.37
	28.12.22	idem						51.0	
XIII	5.4.23	normal	51.0					47.0	
		1 forearm at 45°						51.0	
	7.6.23	normal		67.0	12.22	17.34	29.5		7.15
		1 foot at 43°		60.0	10.40	18.12	42.6		
		2 feet at 43°		58.0	7.88	17.13	54.0		
	20.6.23	normal		62.0	11.78	17.20	31.5		
	4.7.23	1 forearm at 45°		51.4	0.41	17.66	97.6		7.34
	6.7.23	Blood of the right forearm during a bath of the left forearm (45°)		55.5	2.39	18.78	87.2		
IX	10.3.24	normal	51.5	61.7	10.25	17.50	41.5	51.5	7.26
		2 legs at 45°		51.6	1.92	19.86	90.0		7.33
VIII	5.X.23	normal						57.0	
		Blood of the left forearm during a bath of the right forearm (45°)						59.0	
	9.X.23	idem						59.0	
	17.X.23	normal						57.0	
I	7.XI.24	normal		55.9	16.10	20.69	22.1	45.0	7.29
		2 legs at 45°		47.0	2.93	20.44	85.6	55.0	7.43
VII	14.XI.24	2 legs at 45°		62.4	5.07	20.04	74.7		
		normal		68.9	9.10	20.00	54.5		

2) GENERAL ACTION OF LOCAL HOT BATHS.

From the beginning of these experiments I was able to notice the secundary but not less important action of local hot baths.

From the immersion of the fore-arm in a bath at 45°, the pulse increased in frequency, rapidly reached a maximun in some minutes and maintained it during the whole duration of the bath.

On the other hand, when one immersed the left fore-arm into the hot water the veins of the back of the hand and of the right fore-arm and those of the legs and thighs condiderably increased in size, whatever the temperature of the laboratory (+). It was therefore probable that these baths acted upon the general circulation. Different experiments have proved it.

A) GASES OF THE BLOOD.

I) If we place a fore-arm into hot water, the venous blood of this arm not only becomes again arterial, but the venous blood of the opposite arm sees its oxyhoemoglobin saturation increase and its CO2-content diminish (subject 6 and I3, Table I3).

2) A fore-arm being placed in hot water, the dissociation curve of the venous blood of the opposite arm rises (subjects 6 and 8, Table I3).

3) It is well known that, under the preceding conditions, a reflex vasodilatation favours the circulation in the opposite arm, and it was necessary

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(+) During the whole time of the bath the subjects were undressed and the temperature of the room did not vary by I/2 degree.

to ask one's self if this increase of the circulation was not solely limited to this arm. It is not the case; indeed, if we immerse a foot up to the knee into a bath at 43° or 45° the oxyhoemoglobin saturation of the venous blood of the arm increases, and its CO2-content diminishes; if the two feet are immersed the phenomenon is still more accentuated (subjects 9, 8, I and 7, Table I3).

4) Finally, under the same conditions, the alkaline reserve of the blood of the arm rises (subject I, Table I3).

It follows from these different facts that the acceleration of the circulation is general and not solely limited to the arm under experiment nor to the opposite arm. The study of the general blood-flow is a direct proof of it.

B) BLOOD-FLOW.

The general blood-flow is on an average doubled by placing a fore-arm into a bath at 45°. Table I4 shows some absolutely typical examples of it.

Table I4 to be inserted here.

This increase of blood-flow is accompanied by modifications of circulatory and respiratory regime interesting particularly the alveolar air, the tension of the carbonic acid of the mixed venous blood, the expired air, etc.

If we determine the pressure of the alveolar carbonic acid before the hot bath, then in the first few minutes of the bath, we see this pressure rise little by little to reach a maximum (which is maintained in

the majority of cases during the total duration of the experiment) at the end of from 20 to 25 minutes. Table I5 gives some examples of it.(+) It is therefore necessary, in order to obtain a correct figure, to wait 25 minutes before beginning the determination of the blood-flow.

(+) Subject I3 does not belong to the ordinary category of patients suffering from circulatory slowing by reason of the fact that his alveolar CO2 is not decreased. We can explain this anomaly. Indeed, this subject was a manifest hypothyroid (basal metabolism: -20 to-26 %), absolutely apathetic and without the least energy, living in a semi-comatous state. We can admit that under these conditions, his respiratory centre was much less sensitive than with healthy subjects, and that he did not respond by overventilation to the accumulation of carbonic acid in respiratory centre. We observe, indeed, the small quantity of expired air per hour which Table I4 shows regarding this subject.

What confirms this view, is that this subject did not respond to the application of a weak respiratory resistance by overventilation as healthy subjects do (DAUTREBANDE (69)), and that, under these conditions, his alveolar carbonic acid increased without the least respiratory reaction.

Moreover, this hypoexcitability of the centre was not absolute, as in the course of a new fall of the blood-flow this patient saw his alveolar CO2 diminish, his expired air increase in volume, as table I5 bis shows.

Table I5 bis.

Date	Alveolar CO2 %	mmHG	Expired air per hour.	Blood-flow litres per minute.
24-7-23	5,42	38,I	40I	3,48
2-8-23	5,38	37,9	40I	3,67
8-8-23	5,43	38,5	4I8	3,67

As to the tension of the CO2 of mixed venous blood, it falls in a well marked way during the local hot baths; on account of the increase of the blood-flow the carbonic acid does not accumulate any more in so large a quantity in the capillaries as during the stasis, which lowers the pressure of this gas in the mixed venous blood.

The two values (alveolar CO_2 and CO_2 of the mixed venous blood) therefore draw nearer. It is, after all, a phenomenon comparable to that which has been observed in the preceding chapter devoted to the digitalis treatment.

It will finally be observed that 9/IO of the increase of the blood-flow by local hot baths is due to the increase of the systollic flow.

As to the quantity of expired air (table I4), it always increases to an appreciable extent. This increase of ventilation is, apparently, the resultant of several probable causes. It will suffice to note the principal ones: one among them stands clearly out on Table I4: the metabolism increases in rather remarkable proportions. To know exactly the proper influence of the local hot baths on the metabolism I have determined the basal metabolism of Subject 6 at first in the usual conditions, in a comfortable sitting position, then during the immersion of a forearm in a bath at 43°. (+)

(+) and not at 45°, in order to avoid the least dicomfort.

Under these conditions, the metabolism passed from ±0% to + 10%. Before the bath his alveolar air possessed a pressure of 34,8 mmHg CO2 and during the bath (after collecting the expired air) a pressure of 36,8 mmHg. The dead space for carbonic acid was 253 cm3 before the bath, and 266 during the bath. The volume of each respiration was 476 cm3 and 482 respectively. The number of respirations per minute was 19,5 and 20,5 respectively.

On the other hand, the blood which arrives in the medulla oblongata possesses, as we shall soon see, a higher temperature than normally. This factor must act by the intermediary of the respiratory centre on the pulmonary ventilation. C. HEYMANS and LADON (88) have indeed shown that the artificial and progressive increase of the temperature of the blood arriving in the isolated head of a dog increased respiration regularly and progressively.

C) PULSE AND TEMPERATURE OF THE BODY.

It now remains for us to study the influence of local hot baths on the frequency of the pulse and the temperature of the body. During local hot baths, the pulse and the buccal temperature behave in a very peculiar manner, and always the same, with the healthy subjects as with the cardiac patients.

From the first few minutes of the immersion of the arm, the frequency of the pulse already increases in an appreciable way. The pulse reaches its maximum of frequency at the end of from 7 to 10 minutes, then it remains at this maximum during the whole duration of the experiment, however long it be (two hours or

more).

After we have taken the arm from the water, the pulse rapidly slows (sometimes from 10 to 12 beats during the first three minutes) then falls slowly, reaching its starting point in about 15 minutes and infallibly goes below its starting point (5 to 13 beats) 40 to 45 minutes after the end of the bath. Three hours after the bath it has not retaken its original rhythm.

If instead of withdrawing the arm, we let the water cool gradually it is sufficient that the temperature of the water falls from 45 to 42 degrees to see the frequency of the pulse strongly diminish. Near 40° it reaches its starting point and then goes below it even when the bath remains at 39°.

The buccal temperature follows a curve parallel to that of the pulse, but 4 to 5 minutes later. It was determined by means of a very precise thermometer reaching its maximum in one minute. When the arm is immersed into the water the temperature remains unchanged during the first few minutes of the bath. The rising only begins in truth after 6 or 7 minutes, to reach its maximum at the end of 20 minutes on an average.

When we withdraw the arm from the water, the temperature remains at its maximum for 2 or 3 minutes, although the pulse has already fallen considerably, then it falls again but slowly. It returns to its starting point only after 30 minutes on an average. If we let the water cool slowly the buccal temperature can remain at its maximum till the temperature of the bath is below 40°, then it falls again very slowly

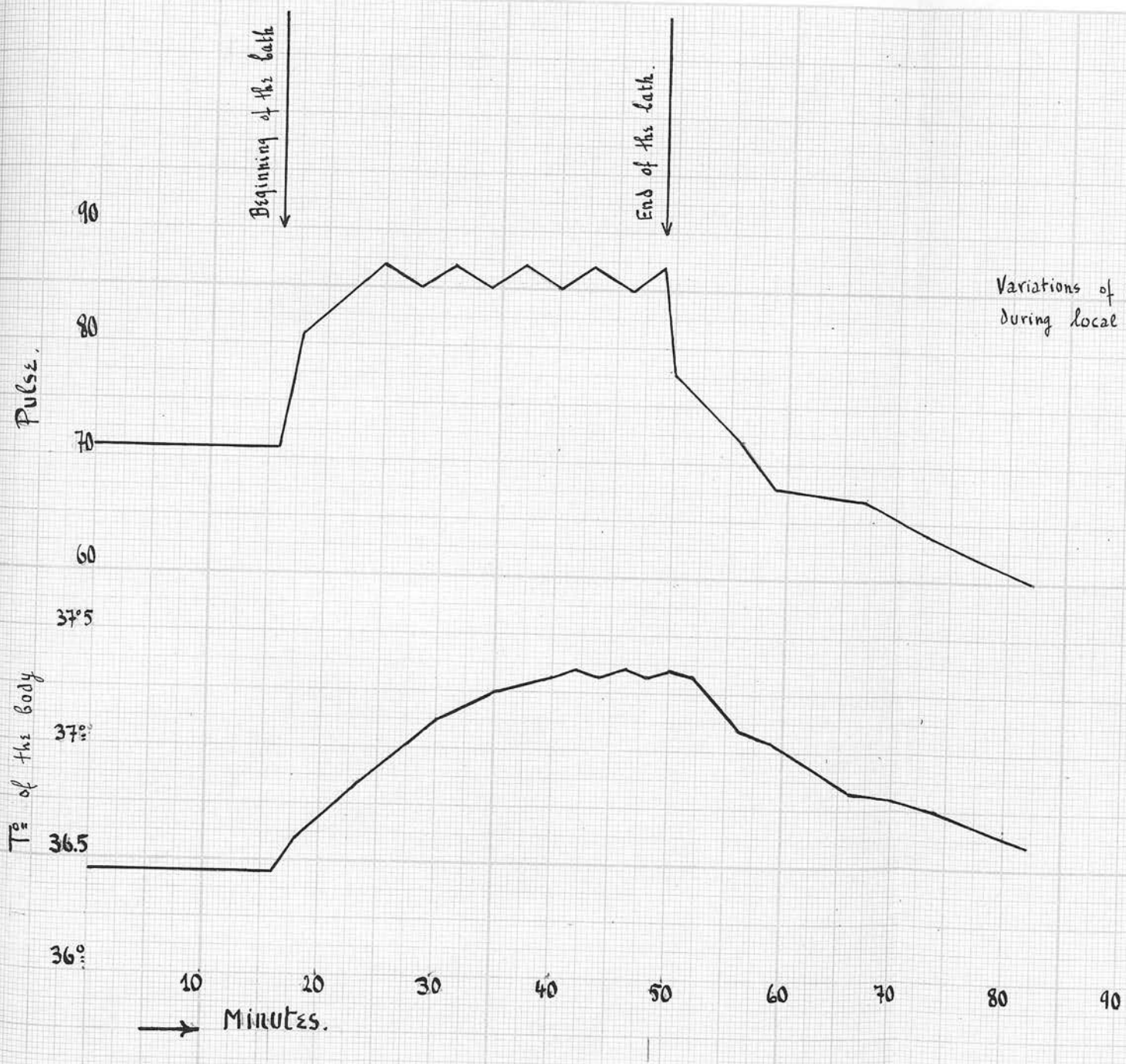

Fig XII

Variations of pulse and body temperature during local warm bath (45°C.)

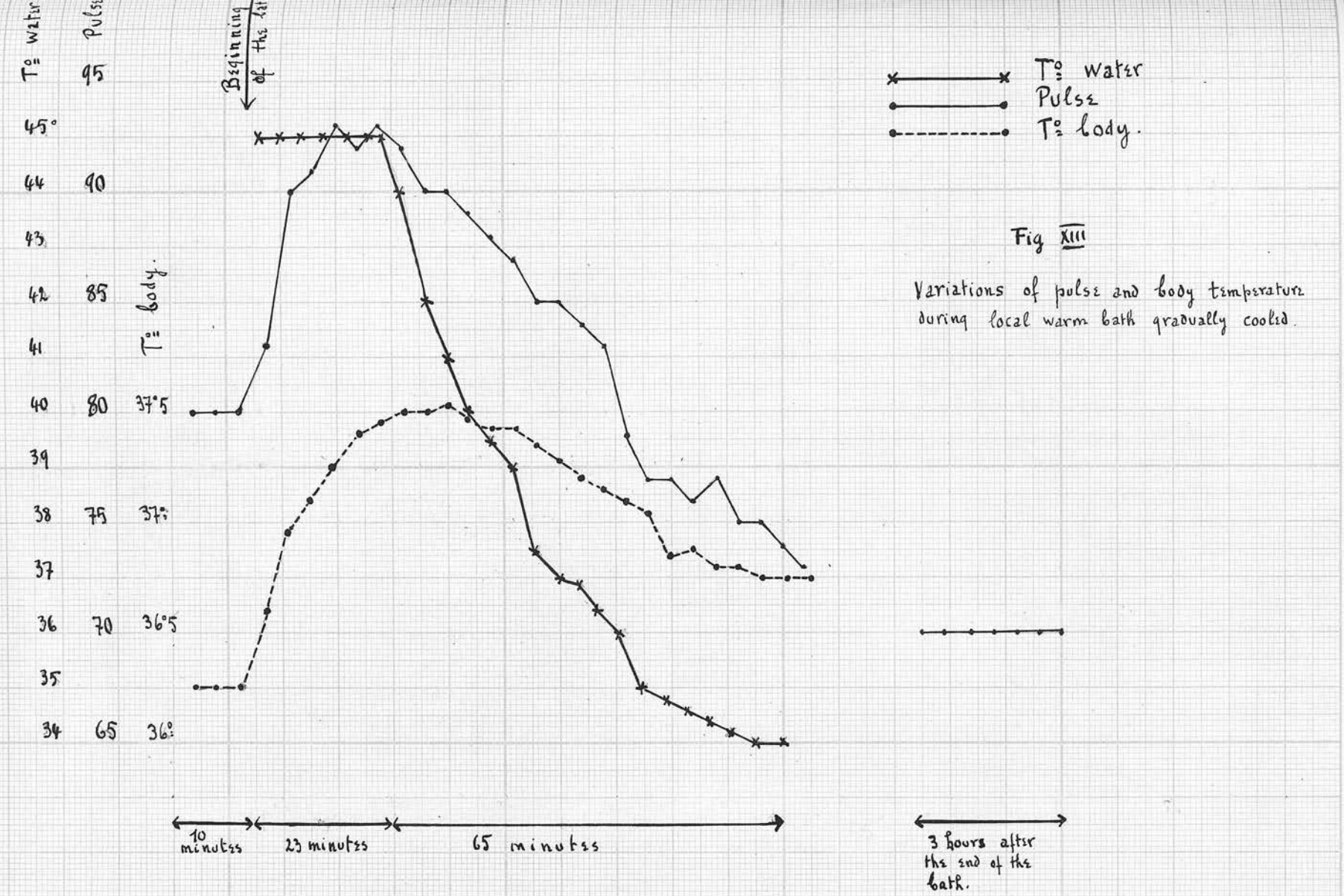

Fig XIII

Variations of pulse and body temperature during local warm bath gradually cooled.

Date	Conditions	Alveolar CO_2	
		%	mmHg
24.5.23	normal	5.86	41.4
29-5-23	1 hand at 40°	6.12	43.3
30.5.23	"	6.05	42.65
27.4.23	1 foot at 45°	6.13	43.0
1-5-23	1 hand at 45°	5.95	42.3
8-6-23	"	6.00	42.6
31-5-23	1 hand at 48°	6.23	44.0
30-5-23	1 forearm at 40°	6.18	43.6
28-5-23	1 forearm at 45°	6.18	43.5

and is still much above its starting point when the water is at 36°.

These rises and falls of the pulse and buccal temperature during and after the bath vary with individuals, and from day to day with the same subject. The temperature can pass, for example, one day from 36,3 to 37,5, and another day only rise from 0.3°.

The figures I2 and I3 refer to the facts studied in this chapter. Figure I2 is the average of 5 observations made on subjects II and I3. Figure I3 represents one of numerous experiments made with subject I3 in the course of a progressive cooling of the bath.

D) VARIATIONS OF THE BLOOD-FLOW ACCORDING OF THE TEMPERATURE OF THE BATH AND THE SIZE OF THE CUTANEOUS SURFACE IMMERSED IN HOT WATER.

It follows from the evidence of Table I6 that the degree of increase of the blood-flow depends upon two important factors.

At first the size of the skin surface submitted to the bath undoubtedly counts. It is thus that in the bath at 45° the flow passes from 4,I2 to 5,4 litres on average if it is the hand or the foot which is immersed in the water, and to 7,4 litres if it is the fore-arm.

The increase of the blood-flow also varies with the temperature of the water. When the hand is immersed in a bath the flow passes to 4,75, 5,3, and 7,9 according to the temperature of the bath being of 40, 45, or 48 degrees respectively.

In the same way, in the course of the immersion of the fore-arm, the flow passes to 5 and to 7 litres

according to the temperature of the bath being of 40 or 45° respectively.

These experiments were made with the same subject in the course of a period during which his blood flow remained remarkable stable. (4,39 litres on 20-4; 4,26 on 25-4; 4,47 on 2-5; and 4,I2 on 24-5-23). (+)

E) H ion CONCENTRATION OF THE ARTERIAL BLOOD AND OF THE VENOUS BLOOD.

The preceding report has sufficiently shown the part played by local hot baths. Under their influence the general circulation is accelerated, the arterial blood is enriched in carbonic acid and the venous blood coming from zones where the stasis has disappeared, sees its CO2-pressure decrease.

The difference existing between the pressure of the arterial carbonic acid and of the carbonic acid of the mixed venous blood therefore diminishes. It follows that the difference between the arterial pH and the venous pH, originally too high, also diminishes. That is what the different figures of Table I7 clearly show.

"

" "

The local hot baths therefore realise experimentally

(+) The rise of the buccal temperature and pulse above the starting point is indicated in the last two colums of Table XVI. These figures represent the average of the figures obtained during the first half-hour of the bath only (to avoid the influence of the normal variations of the pulse and temperature), which explains that this rise is not so considerable as that of figures I2 and I3.

a sharp cardiac recompensation in the patients without valvular lesions.

As to the mode of action of these baths, it seems to be very complex. Nevertheless, we can, from the whole of these experiments, bring to light two factors which appear to play an importan part: I) the temperature of the blood which comes to heart and secondarily the temperature of the body; 2) the increase of the pressure of the returning venous blood.

The work of STARLING and his school have brought to light the function of these three factors.

If we increase the temperature of the liquid of cardiac perfusion the frequency of the pulse is imme diately raised. That is what is shown here: the blood which traverses the parts exposed to the hot water sees its temperature raised and we can say that its temperature at its entering the heart, is higher than normally since the buccal temperature rises progressi-vely.

On the other hand, this rising of the temperature of the body can alone increase the blood-flow. We know indeed that fever accelerates the circulation. We can easily notice it if we analyse the venous blood of a feverish subject; his hoemoglobin is much richer in oxygen than that of the normal venous blood. On the other hand some unpublished observations have shown me that, during fever, the blood-flow was considerably increased in man.

Finally the venous pressure is itself increased. The proof of it is in the dilatation of the peripheral veins of all the

limbs. Another proof is in the fact that the increase of the blood-flow during the hot baths is especially tributary to the increase of the systolic flow. In short, we can by a measure of the venous pressure by means of CLAUDE's manometer directly notice the action of local hot baths. In subject II the pressure of the venous blood of the arm is normally II centimetres of water. Immediately after a bath of a forearm for 20 minutes at 43° it is I4 centimetres. In the opposite arm it is I4 centimetres during the bath. In cardiac patients who do not come in the category of those of the present study, I have been able to observe that the increase of the venous pressure was still more considerable. But the first effect of the increase of the pressure of the returning venous blood is to favour the dilatation of the ventricles and to increase their contractile force (STARLING). As a matter of fact the rising of the temperature increases the dilatation of the heart (EVANS (87)).

Finally, with the cardiac subjects submitted to local hot baths, the oxygenation of the myocardium is better, which can only reinforce the action of the first two factors.

CONCLUSIONS.

I) The local hot baths have not only a local action. A bath of a forearm improves the circulation of the other arm, a foot-bath improves the circulation of the arms.

2) A bath of a forearm at 45° can double the

general blood-flow. The increase of the blood-flow depends upon two principal factors: I) the size of the tegumentary surface immersed; and 2) the temperature of the bath.

3) On account of the increase of the blood-flow the values of the arterial pH and of the venous pH, originally too distant from each other, draw nearer. Thus the local hot baths reproduce the principal phenomenon of the cardiac recompensation.

4) During local hot baths the buccal temperature rises, the temperature of the blood arriving at the heart is higher than normally, and the pressure of the returning venous flow is increased; these three factors apparently constitute the principal cause of the increase of the blood-flow under these conditions.

VIII

GENERAL CONCLUSIONS.

It seems that the different propositions enunciated at the beginning of this work are verified.

I) The characteristics of the blood stasis, namely the venous acidosis and the arterial alkalosis, are found in the different kinds of circulatory slowing, whatever be their origin, pathological or experimental.

2) In the course of the stasis the passage of the bicarbonate of the blood towards the tissues results in the fall of the alkaline reserve, in the arterial as well as in the venous blood.

3) The treatment of the cardiac diseases in causing the blood stasis to disappear makes the arterial alkalosis and the venous acidosis retrocede. The dissociation curve of the carbonic acid, both arterial and venous, returns to its original level.

4) Local hot baths reproduce experimentally the phenomena of cardiac recompensation: the local cold baths are accompanied by numerous phenomena of the cardiac decompensation.

A conclusion of a more general order must result from this thesis: we have seen that in the diseases characterised by a circulatory slowing, the pH of the blood can vary from one part of the body to the other; an acidosis can even coexist in the same organism with an alkalosis. The organism must be considered as a whole reacting locally to variable influences and sometimes of contrary signs. A single pH, arterial or

venous, a simple examination of the urine, a single collection of the alveolar air may not give sufficient indications regarding the reactional state of the whole of the organism. Each function must be studied separately and simultaneously; only confronted results will give an idea of the nature of the general phenomena and their mechanism.

Circulatory troubles are frequent in all kinds of illnesses, and they can, as we have seen, exist in the absence of any clinical sign of decompensation. Therefore we easily understand that under these conditions we risk committing gross errors if we consider only one value of the venous pH and from it draw conclusions concerning the reactional state of the whole organism.

REFERENCES.

I) CHRISTIANSSEN, DOUGLAS & HALDANE Journ.of physiology I9I4, 48, 244.

2) VAN SLYKE & CULLEN Journ of biolog.chemistry, I9I7, 30, 289.

3) L.J. HENDERSON Ergebnis.d.Physiol. I909, 8, 254.

4) J.B.S. HALDANE Journ of Physiol. I92I, 55, 265.

5) MEAKINS & DAVIES Edinburgh ad.journ. october I922.

6) HENDERSON & HAGGARD Journ of biological chem. I9I8, 33, 333.

7) DAUTREBANDE LeScalpel, avril I923 & Bulletin Ligue belge contre la tuberculose, juillet I923.

8) SCOTT Archives Internal medic. I920, 25, 544.

9) HENDERSON & HAGGARD Journ.Biolog.Chemistry I9I8-20 series of papers.

I0) STADELMAN Arc hiv.f.exp. Pathol.u.Pharmac. I883, I7, 4I9.

II) NAUNYN Das diabetes mellitus wien, I906.

I2) BEDDARD, PEMBREY & SPRIGGS LANCET I903, I, I366.

I3) STILLMAN, VAN SLYKE, CULLEN & FITZ Journ.Biolog. Chem. I9I7, 30, 405.

I4) POULTON Goulstonian Lectures. Lancet, june I9I8, 863.

I5) DAVIES LAMBIE LYON MEAKINS & ROBSON Brit.med. Journ, I923, may I9.

I6) CULLEN & JONAS Journ.Biolog.Chem. I923, 57, 54I.

I7) STRAUB & SCHLAYER Munchen.med.Wochens. I9I2, 59, 569.

I8) PEABODY Archives intern.medic. I9I4, I4, 236.

I9) LEWIS RYFFEL WOLF COTTON & BARCROFT Heart I9I3, 45.

20) PALMER & HENDERSON Journ.Biolog.Chem. I9I2-I3, 393; I9I5, 2I, 57.

2I) FETERR Archiv. Imter.medic. I923, 3I, 4I3.

22) MEANS & ROGERS Amer.Journ.medic sciences I9I7, II3, 420.

23) HOWLAND & MARRIOTT Amer.Journ.diseases of Children I9I6, II, 309.

24) SCHLOSS & HARRINGTON Amer.Journ.diseases of Children I9I9, I7, 85.

25) SCHLOSS Amer.Journ.diseases of Children I9I7, I3, 2I8.

26) BENEDICT A study of prolonged fasting Washington, I9I5.

27) FOLIN & DENIS Journ.Biolog.Chem. I9I5, 2I, I83.

28) CATHCART Journ.of Physiol. I906-7, 35, 500.

29) BRUGTSTH Zeits.f.exp.Pathol u Therap. I905, I, 4I9.

30) BOEMINGER & MOHR Zeits.f.exp.Pathol.u. Therap. I906, 3, 675.

3I) KENNAWAY, Biochem. Journal I9I4, 8, 355.

32) LABBE STEVENIN & NEPVEUX Comptes-rendus Soc.Biologie, I922, 87, 602.

33) HASSELBACH & GAMMELTOFT Biochem. Zeitsch. I905, 68, 205.

34) WILLIAMSSON Americ.Journ of obstetrics, september I923.

35) WEISMANN-NETTER Comptes-rendus Soc.Biologie, I924, 90, 94I.

36) LOSEE & VAN SLYKE Americ.Journ. medic.Sciences I9I7, II3, 94.

37) UNDERHILL & RAND Archiv Intern.medic. I9I0, 6I.

38) SELLARDS Bul.Johns Hospit. I9I2, 23, 289.

39) GILLIAT & KENNAWAY Quartely Journ of medic. I9I9, I2, 6I.

40) WILLIAMS Bullet.Johns Hopkins Hosp. I906, I7, 7I & Journal med.Sciences I906, I32, 343.

4I) DAVIES HALDANE & KENNAWAY Journ.of.Physiol. I920, 54, 32.

42) HENDERSON & HAGGARD Journ.Biolog.Chem. I920, 45, 209 & 2I9.

43) HALDANE & PRIESTLEY Journ.of Physiol. I905, 32, 225.

44) GURBER Sitzungsb.med.phys.Ges. I895, 28.

45) HAMBURGER Zeits.f.Biolog.I89I, 28, 405 & Biochem. Zeits. I9I8, 86, 309.

46) FRIDIRICIA Journ.Biolog.Chem.I920, 42, 243.

47) DOISY & EATON Journ.Biolog.Chem. I92I, 47, 377.

48) DAUTREBANDE & DAVIES Journ of Physiol. I922, 57, 36.

49) HALDANE KELLAS & KENNAWAY Journ.of Physiol. I9I9, 53, I8I.

50) HASSELBACH & LINDHARD Biochem.Zeits. I9I5, 68, 265 & I9I6, 74, 48.

5I) BEDDARD & PEMBREY British med.Journ, I908, 2, 580.

52) FITZGERALD Journ.of Pathol. & Bacteriol. I9I0, I4, 328.

53) PORGES LEIMDORFER & MARKOVICI Zeits.f.klin.Med. I9I3, 77, I46.

54) PETERS & BARR Americ.Journ.Physiol. I920, 54, 307.

55) PETERS " " " . I9I7, 43, II3.

56) CAMPBELL & POULTON Journ.of Physiolog.I920-2I, 54. Proceed. Physiolog.soc., p 49.

57) MEAKINS DAUTREBANDE & FETTER. Heart I923, I0, I53.

58) DAUTREBANDE Bul.Académie royale de médec. de Belgique avril I924 & Bul. Soc. des sciences nat & méd. de Bruxelles, 8, october I924.

59) NEWBURG PALMER & HENDERSON Archiv. Intern. Med. I9I3, I2, I46.

60) HARROP Journ exper. med. I9I9, 30, 24I.

6I) FRASER ROSS & DREYER Quarterly Journ med I922, 59, I93.

62) DAUTREBANDE DAVIES & MEAKINS Heart, I923, I0, I33.

63) FLETCHER & HOPKINS Journ of Physiol. I907, 25, 247.

64) BARCROFT The respiratory functions of the blood Cambridge I9I4.

65) DOUGLAS & HALDANE Journ. of Physiol. I922, 56, 69.

66) HENDERSON Physiolog. Reviews I923, 3, I65.

67) MEAKINS & DAVIES Heart, I922, 9, I9I.

68) DAUTREBANDE & DAVIES Edinburgh med.Journ., october I922 & Bulletin Académie de médecine de Belgique, april I922.

69) DAUTREBANDE Comptes-rendus séance plénière soc. Biologie june I924, - I83.

70) HENDERSON & PRINCE Journ. Biolog. Chemist. I9I7, 33, 325.

71) PARSONS Journ.of Physiol. I9I9, 53, 42.

72) BARCROFT & MARSHALL Journ.of Physiol. I923, 58, I45.

73) C.L.EVANS Journ.of Physiol. I922, 56,I46.

74) HALDANE Journ. of Pathology & Bacteriology. I920, 23, 443.

75) HASSELBACH Biochem Zeits. I9I6-I7, 77, II2.

76) PETERS BARR & RULE Journ.Biolog.Chemist. I92I, 45, 438.

77) DOISY BRIGGS EATON & CHAMBERS Journ.Biolog. Chemistry I922,54, 305.

78) PARSONS Journ. of Physiol. I9I7, 5I, 440.

79) BIGWOOD Comptes-rendus soc.Biologie, I923, 88, 639.

80) LUNDSGAARD Journ.Experim.Med.I9I8, 27, I79.

8I) WRIGHT & COLEBROOK Comptes-rendus conférence chirurg.interalliée pour l'étude des plaies de guerre, march I9I8. Fournier, Paris, editor.

82) MEAKINS & DAVIES Journ of Pathol. & Bacteriol. I9I9-20, 23, 45I.

83) GOLDSMIDT & LIGHT Abstracts physiolog. Congress, Edinburgh july I923.

84) in von NOORDEN Pathology of metabolism, 968. Walker Hall editor.

85) DOUGLAS & HALDANE Journ of Physiol. I9I2, 45, 23I.

86) DAUTREBANDE Comptes-rendus séance plénière soc. biol. june I924, I87.

87) EVANS Journ of Physiol. I9I7, 5I, 9I.

88) HEYMANS & LADON Comptes-rendus soc. de biologie, I925, 92, 455.